AIR FORCE HEALTH STUDY

An Epidemiologic Investigation of
Health Effects in Air Force Personnel
Following Exposure to Herbicides

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CHAPTER 12

PSYCHOLOGICAL ASSESSMENT

INTRODUCTION

Background

Although some epidemiologic studies in humans have associated chronic psychologic disorders with the perception of herbicide exposure (1), a direct causal relationship implicating 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD, or dioxin) has not been proven. Experimental animal studies provide little insight into potential psychological consequences of TCDD exposure in humans. Signs of toxicity in animals (lethargy, stupor, poor coordination, lack of feeding, and agitation) have been observed in multiple studies involving many species and have been attributed to the "wasting syndrome" of multi-organ toxicity rather than to primary central nervous system (CNS) toxicity (2). In rats exposed to high doses of TCDD (1,000 micrograms intraperitoneally), only slight differences were noted in spontaneous motor activity and maze performance relative to controls (3).

Experiments in monkeys exposed perinatally to TCDD may be more relevant to human experience. Several published reports have documented behavioral dysfunction and subtle cognitive impairment in monkeys exposed to TCDD (by maternal ingestion) while in utero and during nursing (4-6).

Studies attempting to define human psychological and behavioral disorders related to TCDD exposure often are flawed by a number of limitations including the bias of self-reporting, the lack of confirmation by psychological testing, and unreliable indices of exposure. Using chloracne as a marker for high-level exposure, early studies of industrial chemical workers provided the first suggestion of psychological effects. Studies shortly after a Nitro, West Virginia, accident in 1949 documented nervousness, fatigue, irritability, cold intolerance, and decreased libido in many of the workers with chloracne. Most of these symptoms resolved over a 4-year period (7,8). Two followup studies of expanded plant cohorts in 1979 noted a strong association between chloracne and insomnia (9,10). None of the studies included validation by neurobehavioral testing.

Other industrial-based studies reported a wide range of acute and subacute subjective symptoms including fatigue, decreased libido, impotence, sleep disturbances, reduced emotional responses, sensory deficits, reading difficulties, memory loss, and emotional disorders (11-17). One study found a relationship between chloracne and hypomania as reflected in the Minnesota Multiphasic Personality Inventory (MMPI) (18). Another study noted that two of three chemists involved in the synthesis of TCDD developed marked personality changes (19). Although data interpretation problems exist, a Czechoslovakian 10-year followup study cited eight cases of severe dementia in exposed workers and reported that symptoms of anxiety and depression decreased over the followup period (17).

A contemporary cross-sectional morbidity study of residents of a mobile-home park environmentally contaminated with dioxin documented psychological changes in the exposed group (20). Significant abnormalities were recorded in the exposed group for the tension or anxiety scale and the anger or hostility scale of the Profile of Mood States Inventory as well as the vocabulary subtest of the Wechler Adult Intelligence Scale (WAIS). However, cerebral function, as assessed by the Halstead-Reitan Battery (HRB), revealed no significant group differences.

As one of the few epidemiologic studies in humans to incorporate serum dioxin data into psychometric analyses, the National Institute for Occupational Safety and Health (NIOSH) study of chemical plant workers deserves special mention (21). This cross-sectional study of 281 workers in two industrial plants investigated the association between exposure to chemicals (including TCDD) and symptoms of depression revealed by a well-established battery of psychologic screening tests (the Beck Depression Inventory and the depression subscale of the Symptom Checklist-90-Revised [SCL-90-R]). The mean serum TCDD level in the exposed cohort was 220 parts per trillion (ppt) versus 6 ppt in referents. By both scales the prevalence of depression was comparable in each group. Of interest and consistent with numerous other reports, the self-perception of TCDD exposure was significantly associated with depressive symptoms though the mean serum TCDD level in those thought to have been exposed (43 ppt) was significantly lower than that in the group reporting no such exposure (116 ppt).

The association of psychological symptoms with the self-perception of exposure to Agent Orange was reported in a Veterans' Administration study of 153 veterans undergoing treatment for substance abuse (22). Though no attempt was made to document actual exposure objectively, a subgroup of 58 patients self-reporting moderate to high herbicide exposure was compared to the remaining 95 patients reporting no or minimal exposure. When adjusted for age, education, and degree of combat experience, the self-perceived exposed group scored significantly higher in the MMPI scales of depression, poor morale, organic symptoms, family problems, and hypomania.

In addition to unreliable herbicide exposure estimates, the study of psychopathology in veterans is further complicated by the confounding effects of combat stress and post-traumatic stress disorder (PTSD) as defined by the American Psychiatric Association (23). Though the true prevalence of PTSD in Vietnam veterans is uncertain (24,25), 18 percent of the nearly 100,000 Vietnam veterans registered in the Veterans' Administration Agent Orange Registry in 1983 complained of "nervousness," and 10 percent reported personality disorders (26). In a group of 132 veterans included in the registry (most of whom were selected for inclusion in the study based on referral for psychotherapy), 53 percent met criteria for PTSD based on symptoms of sleep disorders (53%), mood depression (36%), suicidal thoughts (35%), and irritability (31%) (27). Many studies have attempted to investigate the relationship between PTSD and herbicide exposure in Vietnam veterans. The methods employed to determine exposure included self-reporting, use of chloracne symptoms (both self-reported and medically diagnosed), and various attempts to link the geographic location of a veteran during service in Vietnam to areas of herbicide use. All of these methods have questionable validity. Self-reporting has been shown to be highly inaccurate for most applications (28). One study in which chloracne was used as an index of exposure

examined six Vietnam veterans and 25 control subjects selected from the same sample group. Evidence was found for significant psychological disorders in the exposed subjects based on the results of a neuropsychological battery (29). Principal limitations of the study included the small sample size and lack of histologic confirmation of chloracne diagnosis.

Another large-scale study of 6,810 Vietnam-era veterans who are members of the American Legion found that, although perceived exposure to herbicides could not independently predict psychosocial outcomes, it was associated with such outcomes when combined with combat, indicating that a synergistic effect may have occurred (30). Principal limitations of the study include the lack of medical and psychological record review and exposure verification.

Although not specifically designed to investigate endpoints from Agent Orange exposure, the Vietnam Experience Study (VES) by the U.S. Centers for Disease Control, included comprehensive psychological testing in Vietnam and non-Vietnam veterans (31). Results revealed an increased incidence of psychological dysfunction related to service in Vietnam including depression (4.5% of Vietnam veterans versus 3.2% in non-Vietnam veterans), anxiety (4.9% versus 3.2%), and alcohol abuse or dependence (13.7% versus 9.2%).

Prior reports of the Air Force Health Study (AFHS) (32-34) have revealed few statistically significant differences in the psychologic indices between the Ranch Hand and Comparison cohorts. Furthermore, in the most recent analyses based on serum dioxin levels (35), psychological and psychosocial disorders in Ranch Hands appear unrelated to the body burden of TCDD.

Summary of Previous Analyses of the Air Force Health Study

1982 Baseline Study Summary Results

An extensive battery of psychological parameters was assessed on all participants during the 1982 Baseline questionnaire and physical examination. The expected high degree of concordance between education (college, high school) and military rank (officer, enlisted) was observed and validated the use of education as the sole covariate representing socioeconomic status for most analyses.

There were no questionnaire differences for past history of emotional or psychological illnesses between the Ranch Hand and Comparison groups. For the psychological indices of fatigue, anger, erosion, anxiety, and severity of depression (as determined by a modification of the Diagnostic Interview Schedule), no group differences were detected among the college-educated Ranch Hands. However, for the high-school-educated stratum, Ranch Hands demonstrated significantly more fatigue, anger, erosion, and anxiety. An unadjusted analysis of reported depression showed significantly more depression in the Ranch Hands, as did the isolation index adjusted for educational level.

At the time of the physical examination, additional self-reported data were collected with the Cornell Index and the MMPI. The CNS functional testing was conducted by a modified HRB, and intelligence was measured by the WAIS.

The Cornell Index showed a significant increase in psychophysiologic symptoms in the high school-educated Ranch Hands. In Ranch Hands, 6 of 10 parameters of the Cornell Index were abnormal (e.g., fear, startle, psychosomatic), as contrasted to the Comparisons, and all abnormal responses and parameters were inversely related to education to a statistically significant degree. MMPI results in the high-school-educated participants showed differences in the scales of denial, hypochondria, masculinity-femininity, and mania-hypomania as contrasted to the college-educated participants. Only the social introversion scale was significant in the college-educated participants. The effect of education was influential ($p<0.01$) in all scales of the MMPI. Race was not a significant covariate. None of the self-reported data, including those from the in-home questionnaire, were adjusted for possible group differences in PTSD or combat experience and intensity.

Performance testing by the HRB showed no neuropsychiatric impairment in the Ranch Hands in contrast to the results of the self-administered MMPI and the Cornell Index. The effect of education on the HRB testing was strong ($p<0.0001$). WAIS intelligence scores revealed very close group similarities in the full-scale and verbal and performance scales. As expected, the intelligence quotient (IQ) of college graduates was significantly higher than the IQ of high school graduates.

1985 Followup Study Summary Results

Two of the psychological tests (MMPI, HRB) conducted at the 1982 Baseline examination were repeated at the first followup examination in 1985. An updated history of mental and emotional disorders and combat experience in Vietnam also was obtained on all participants. An indicator of PTSD was derived from a new MMPI subscale and was used for covariate adjustments of non-MMPI psychological data. The Cornell Medical Index (CMI) was substituted for the Cornell Index in the 1985 psychological assessment. Questionnaire data (verified by medical record reviews) for the lifetime events of psychotic illness, alcohol dependence, anxiety, or other neuroses disclosed no significant differences between groups for these conditions.

The similarity of the group distribution for the 14 MMPI variables, each stratified by the 3 occupational categories, was examined, and only 2 of the 42 tests approached statistical significance (masculinity-feminity for enlisted flyers and validity for officers). The group distributions of the total CMI score were similarly contrasted, with separate analyses performed with stratification by the five covariates of age, race, occupation, education, and current alcohol drinking status. For one stratum of each of these covariates (born in or after 1942, non-Black, enlisted groundcrew, high school education, and current alcohol drinker), a significant difference in the distribution of the Ranch Hand and Comparison scores was found. In all cases for the CMI, the Ranch Hand mean was greater than the Comparison mean.

The unadjusted analyses showed a significant difference for the MMPI scales of denial ($p<0.001$) and masculinity-femininity ($p=0.017$), the total CMI ($p<0.001$), and the Section A-H area subscore ($p=0.003$). A marginally significant difference was observed for the MMPI scales of hysteria ($p=0.067$) and social introversion ($p=0.069$). Comparisons had a greater percentage of abnormal scores for the denial and masculinity-femininity scales, whereas Ranch Hands showed adverse findings for the other four variables.

The adjusted analyses were generally quite similar to the unadjusted analyses with respect to group differences. The MMPI scales of denial and masculinity-femininity were statistically significant in both the adjusted and unadjusted analyses, where Comparisons showed an adverse effect over Ranch Hands. The A-H subscore of the CMI (suggesting diffuse medical problems) also was significant, where Ranch Hands had higher mean scores than Comparisons, suggesting that Ranch Hands had more illness. The M-R subscore of the CMI, a broad indicator of emotional health, was not statistically different between the two groups.

The HRB impairment index, a measure of CNS functional integrity, did not differ significantly between the Ranch Hand and Comparison groups. Strong covariates in the adjusted analysis were age, race, and education.

Because of alternate statistical models and slightly different psychological testing parameters, a direct contrast between the psychological results of the Baseline and 1985 followup examinations was not always possible. However, several broad patterns were observed: the discordance between distributional tests and results from traditional statistical models of the MMPI variables was noted with data from both examinations; there was a narrowing of group differences at the 1985 followup examination for most subjective variables, either by a decrease in Ranch Hand reporting, or by an increase in Comparison reporting; and as at the Baseline, functional CNS testing, as measured by the HRB impairment index, showed no group differences, and did not support an organic basis for differences in self-reported symptomatology. The longitudinal analysis of two MMPI scales, depression and denial, showed a significant reversal of depression seen at Baseline in the high-school-educated Ranch Hands—the number of depression abnormalities decreased in Ranch Hands and increased in Comparisons.

The determination of PTSD in both Air Force cohorts by a relatively new MMPI scale showed a prevalence rate of less than 1 percent. This low rate is strongly influenced by characteristics of the study population (e.g., age, education, and officer ratio).

In conclusion, significant test results were present in both groups or were noted in specific subgroups of a covariate. Educational level, age, and alcohol use showed strong effects on the psychological scales and scores in this psychological assessment. Tests of the CNS by the HRB demonstrated an almost identical prevalence of abnormality in both groups.

1987 Followup Study Summary Results

The psychological assessment was based on verified psychological disorders, reported sleep disorders, and two clinical psychological tests—the SCL-90-R and the Millon Clinical

Multiaxial Inventory (MCMI). The verified data on lifetime psychological disorders showed no group differences for psychoses, drug dependence, and anxiety. However, marginally more Ranch Hands than Comparisons had a verified history of alcohol dependence and "other neuroses" based on unadjusted analyses. The Ranch Hands reported experiencing great or disabling fatigue during the day and talking in their sleep more frequently than the Comparisons. No group differences were detected in the other 13 sleep disorder variables in the unadjusted analyses. Although no significant differences between the Ranch Hands and the Comparisons were found in the unadjusted analyses of the 12 SCL-90-R variables, the Ranch Hands had marginally more abnormalities than the Comparisons for depression, somatization, and an index of the general severity of symptoms. The results of the unadjusted analyses of the MCMI scores revealed that the Ranch Hands had significantly higher mean antisocial and paranoid scores than the Comparisons. Marginally significant differences were identified on the narcissistic and psychotic delusion scores, where the mean score of the Ranch Hands exceeded that of the Comparisons. After adjustment for the covariates, a significant difference remained on the narcissistic score. The Comparisons had a significantly higher mean dependent score than the Ranch Hands.

Serum Dioxin Analysis of 1987 Followup Study Summary Results

In general, the results of the analyses of the verified psychological disorders, reported sleep disorders, and the SCL-90-R variables did not reveal significant associations with initial dioxin or current dioxin and time since tour of duty or find significant differences among the four current dioxin categories. In contrast, several of the analyses of the MCMI variables displayed significant results. However, there was a lack of consistency across similar variables included in the SCL-90-R, MCMI, and reported information. Additionally, the continuous scale of the MCMI variables allowed for a greater ability to detect small differences in the mean MCMI scores than the capability of the discrete analyses of the other three psychological abnormalities. In conclusion, the body burden of dioxin does not appear to be related to psychological or psychophysiological disorders.

Parameters of the Psychological Assessment

Dependent Variables

Data collected through the SCL-90-R were used in the psychological assessment. Additionally, psychological disorders, as verified through medical records review, were used to supplement the psychological evaluation for the 1992 followup.

Medical Records Data

At the face-to-face interview of the 1992 examination, each participant was asked whether he has had a mental or emotional disorder since the date of his last interview. Reported disorders for which treatment was obtained were subsequently verified by reviews of medical records. Information on verified psychological disorders from the 1992 examination was combined with information on verified disorders from the Baseline, 1985 followup, and 1987 followup examinations, and a series of dependent variables regarding verified history of psychological disorders were created. In particular, the verified histories

of psychoses, alcohol dependence, drug dependence, anxiety, and an International Classification of Diseases, 9th Edition, Clinical Modification (ICD-9-CM) diagnostic code-based category of "other neuroses" (ICD codes 300-302, 305-309, and 311) were studied.

Participants with a verified pre-Southeast Asia (SEA) history of a psychological disorder were excluded from the analyses pertaining to that disorder. Additionally, participants who tested positive for the human immunosuppressant virus (HIV) were excluded from all analyses of these variables.

Physical Examination Data

The SCL-90-R, used by the AFHS at the 1987 followup, was used again in the psychological assessment. The SCL-90-R is a multidimensional self-reported symptom inventory designed to measure symptomatic psychological distress in terms of nine primary symptom dimensions and three global indices of distress (36). Each participant was asked to respond to 90 questions in terms of a 5-point scale as follows: 0=not at all, 1=a little bit, 2=moderately, 3=quite a bit, and 4=extremely. Responses were grouped into the nine primary symptom categories, and a raw score for a participant for a category was determined by adding the scores of the answered questions in that category and dividing by the number of answered questions in that category. The raw scores then were converted to T-scores (reference scores for a given population norm) for analysis. These nine categories are anxiety, depression, hostility, interpersonal sensitivity, obsessive-compulsive behavior, paranoid ideation, phobic anxiety, psychoticism, and somatization. These symptom categories are defined in Appendix H-1.

The following three global indices also were analyzed: the global severity index (GSI), the positive symptom total (PST), and the positive symptom distress index (PSDI). The GSI is defined as the sum of the scores of all answered questions divided by the number of answered questions on the entire test. This index combines information on the number of symptoms and the intensity of distress. The PST is the number of questions to which the participant responds positively (i.e., on the 5-point scale, responses 1, 2, 3, or 4). The PSDI is determined by adding the scores of all answered questions and dividing by the PST. This index describes the intensity of the positive symptoms. Each of these indices also were converted to a T-score. The T-scores for the nine primary symptom dimensions and the three global indices were then classified as high or normal, where high is defined as a T-score of 63 or greater (36). All participants were included in the analyses of the nine primary symptom dimensions and the three global indices of distress, including those participants who responded "not at all" to all 90 questions. These indices are described more fully in Appendix H-1.

Participants who tested positive for HIV were excluded from the analysis of the SCL-90-R variables.

Covariates

Covariates examined in the adjusted statistical analyses of the psychological assessment included age, race, military occupation, education level (high school, college), current alcohol use (drinks/day), lifetime alcohol history (drink-years), current total household income, current employment (yes, no), current marital status (married, not married), current parental status (currently having a child under the age of 18: yes, no), and combat service (number of days). Age, current alcohol use, lifetime alcohol history, current total household income, and combat service were used in the continuous form for modeling purposes for general linear models and logistic regression analyses. Current total household income information was collected in the questionnaire in categories with $5,000 increments, between $5,000 and $100,000. The midpoint of each category was used as the current total household income, with $100,000 used for the $100,000 or more category. Educational level, current employment, current parental status, and marital status are all based on self-reported information from the questionnaire. Covariates were discretized as necessary for tabular presentations of covariate interactions with group or dioxin.

The lifetime alcohol history and current alcohol use covariates were based on self-reported information from the 1992 questionnaire and combined with similar information gathered at the 1987 followup. For lifetime alcohol history, the respondent's average daily alcohol consumption was determined for various drinking stages throughout his lifetime, and an estimate of the corresponding total number of drink-years (1 drink-year=365 drinks) was derived. The current alcohol use covariate was based on the average number of drinks per day for the month prior to completing the questionnaire. These covariates were not used in adjusted analyses for the alcohol dependence variable.

For the historical dependent variables based on medical records data, the covariates based on current condition (current total household income, current employment, current marital status, and current parental status) are used as surrogate information to describe the participant's life experience. Current alcohol use was examined in the analyses of the psychological examination variables only. This covariate could not affect the results of a variable based on post-SEA history, and lifetime alcohol history is used to investigate the cumulative effects of alcohol.

Statistical Methods

Chapter 7, Statistical Methods describes the basic statistical methods used throughout this report. The modeling strategy was modified for the adjusted analyses of the psychological endpoints. For these variables, only the covariate main effects and group-by-covariate or dioxin-by-covariate interactions were examined; the pairwise covariate interactions were not investigated because of the large number of covariates.

Table 12-1 summarizes the statistical analyses performed for the 1992 psychological assessment. The first part of this table lists the dependent variables analyzed, data source, data form, cutpoints, candidate covariates, and statistical analysis methods. The second part of this table provides a description of candidate covariates examined. Abbreviations used in the body of the table are defined at the end of the table.

Table 12-1.
Statistical Analyses for the Psychological Assessment

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analyses
Psychoses	MR-V	D	Yes No	AGE,RACE,OCC, DRKYR,EDUC, INC,EMPLOY, MARITAL, PARENT, COMBDAYS	U:LR,CS A:LR
Alcohol Dependence	MR-V	D	Yes No	AGE,RACE,OCC, EDUC,INC, EMPLOY, MARITAL, PARENT, COMBDAYS	U:LR,CS A:LR
Drug Dependence	MR-V	D	Yes No	AGE,RACE,OCC, DRKYR,EDUC, INC,EMPLOY, MARITAL, PARENT, COMBDAYS	U:LR,CS A:LR
Anxiety	MR-V	D	Yes No	AGE,RACE,OCC, DRKYR,EDUC, INC,EMPLOY, MARITAL, PARENT, COMBDAYS	U:LR,CS A:LR
Other Neuroses	MR-V	D	Yes No	AGE,RACE,OCC, DRKYR,EDUC, INC,EMPLOY, MARITAL, PARENT, COMBDAYS	U:LR,CS A:LR
SCL-90-R Anxiety	PE	D	High: $T \geq 63$ Normal: $T < 63$	AGE,RACE,OCC, ALC,DRKYR, EDUC,INC, EMPLOY, MARITAL, PARENT, COMBDAYS	U:LR,CS A:LR
SCL-90-R Depression	PE	D	High: $T \geq 63$ Normal: $T < 63$	AGE,RACE,OCC, ALC,DRKYR, EDUC,INC, EMPLOY, MARITAL, PARENT, COMBDAYS	U:LR,CS A:LR

Table 12-1. (Continued)
Statistical Analyses for the Psychological Assessment

Variable (Units)	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analyses
SCL-90-R Hostility	PE	D	High: T≥63 Normal: T<63	AGE,RACE,OCC, ALC,DRKYR, EDUC,INC, EMPLOY, MARITAL, PARENT, COMBDAYS	U:LR,CS A:LR
SCL-90-R Interpersonal Sensitivity	PE	D	High: T≥63 Normal: T<63	AGE,RACE,OCC, ALC,DRKYR, EDUC,INC, EMPLOY, MARITAL, PARENT, COMBDAYS	U:LR,CS A:LR
SCL-90-R Obsessive-Compulsive Behavior	PE	D	High: T≥63 Normal: T<63	AGE,RACE,OCC, ALC,DRKYR, EDUC,INC, EMPLOY, MARITAL, PARENT, COMBDAYS	U:LR,CS A:LR
SCL-90-R Paranoid Ideation	PE	D	High: T≥63 Normal: T<63	AGE,RACE,OCC, ALC,DRKYR, EDUC,INC, EMPLOY, MARITAL, PARENT, COMBDAYS	U:LR,CS A:LR
SCL-90-R Phobic Anxiety	PE	D	High: T≥63 Normal: T<63	AGE,RACE,OCC, ALC,DRKYR, EDUC,INC, EMPLOY, MARITAL, PARENT, COMBDAYS	U:LR,CS A:LR
SCL-90-R Psychoticism	PE	D	High: T≥63 Normal: T<63	AGE,RACE,OCC, ALC,DRKYR, EDUC,INC, EMPLOY, MARITAL, PARENT, COMBDAYS	U:LR,CS A:LR

Table 12-1. (Continued)
Statistical Analyses for the Psychological Assessment

Variable (Units)	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analyses
SCL-90-R Somatization	PE	D	High: T≥63 Normal: T<63	AGE,RACE,OCC, ALC,DRKYR, EDUC,INC, EMPLOY, MARITAL, PARENT, COMBDAYS	U:LR,CS A:LR
SCL-90-R Global Severity Index (GSI)	PE	D	High: T≥63 Normal: T<63	AGE,RACE,OCC, ALC,DRKYR, EDUC,INC, EMPLOY, MARITAL, PARENT, COMBDAYS	U:LR,CS A:LR
SCL-90-R Positive Symptom Total (PST)	PE	D	High: T≥63 Normal: T<63	AGE,RACE,OCC, ALC,DRKYR, EDUC,INC, EMPLOY, MARITAL, PARENT, COMBDAYS	U:LR,CS A:LR
SCL-90-R Positive Symptom Distress Index (PSDI)	PE	D	High: T≥63 Normal: T<63	AGE,RACE,OCC, ALC,DRKYR, EDUC,INC, EMPLOY, MARITAL, PARENT, COMBDAYS	U:LR,CS A:LR

Covariates

Variable (Abbreviation)	Data Source	Data Form	Cutpoints
Age (AGE)	MIL	D/C	Born ≥1942 Born <1942
Race (RACE)	MIL	D	Black Non-Black
Occupation (OCC)	MIL	D	Officer Enlisted Flyer Enlisted Groundcrew
Current Alcohol Use (ALC) (drinks/day)	Q-SR	D/C	0-1 >1-4 >4

Table 12-1. (Continued)
Statistical Analyses for the Psychological Assessment

Covariates

Variable (Abbreviation)	Data Source	Data Form	Cutpoints
Lifetime Alcohol History (DRKYR) (drink-years)	Q-SR	D/C	0 >0-40 >40
Education (EDUC)	Q-SR	D	College High School
Current Total Household Income (INC)	Q-SR	D/C	≤$55,000 >$55,000
Current Employment (EMPLOY)	Q-SR	D	Yes No
Current Marital Status (MARITAL)	Q-SR	D	Married Not Married
Current Parental Status (PARENT)	Q-SR	D	Child <18 years old No child <18 years old
Combat Service (COMBDAYS)	MIL	D/C	<360 days ≥360 days

Abbreviations

Data Source:	LAB	=	1992 laboratory results
	MIL	=	Air Force military records
	MR-V	=	Medical records (verified)
	PE	=	1992 physical examination
	Q-SR	=	Health questionnaire (self-reported)
Data Form:	C	=	Continuous analysis only
	D	=	Discrete analysis only
	D/C	=	Appropriate form for analysis (either discrete or continuous)
Statistical Analyses:	U	=	Unadjusted analyses
	A	=	Adjusted analyses
	L	=	Longitudinal analyses
Statistical Methods:	CS	=	Chi-square contingency table analysis (continuity-adjusted for 2x2 tables)
	LR	=	Logistic regression analysis

Dependent variable data were missing for some participants. The number of participants with missing data and the number of participants excluded due to pre-SEA conditions or because they tested positive for HIV are provided in Table 12-2.

Analyses of data collected at the 1987 followup study indicated that dioxin was associated with military occupation. In general, enlisted personnel had higher levels of dioxin than officers, with enlisted groundcrew having higher levels than enlisted flyers. Consequently, adjustment for military occupation in statistical models using dioxin as a measure of exposure may improperly mask an actual dioxin effect. However, occupation also can be a surrogate for socioeconomic effects. Failure to adjust for occupation could overlook important risk factors related to lifestyle. If occupation was found to be significantly associated with a dependent variable in the 1992 followup analyses and was retained in the final statistical models using dioxin as a measure of exposure, the dioxin effect was evaluated in the context of two models. Analyses were performed with and without occupation in the final models to investigate whether conclusions regarding the association between the health endpoint and dioxin differed.

The results of the analyses without occupation are presented in Appendix H-3 and are only discussed in the text if the level of significance differs from the original final adjusted model (significant versus nonsignificant).

RESULTS

Dependent Variable-Covariate Associations

Tests of association between the psychological dependent variables and the candidate covariates were conducted, and results are presented in Appendix Table H-1-1. These associations are based on combined group data. Participants with a verified pre-SEA history of a psychological disorder were excluded from the analyses pertaining to that disorder. Additionally, participants who tested positive for the HIV virus were excluded from all analyses.

History of psychoses was found significantly associated only with current marital status ($p<0.001$). The greater history was among participants who were not currently married at the time of the examination.

History of alcohol dependence was significantly associated with occupation ($p=0.009$), with the highest percentage among the enlisted flyers. Participants with only a high school education displayed a higher history of alcohol dependence ($p=0.007$), as did those participants with a current total household income less than or equal to $55,000 ($p<0.001$). The higher history of alcohol dependence was among those participants not currently married ($p<0.001$). Participants who were not married at the time of the examination also demonstrated a significantly higher history of drug dependence ($p=0.022$).

Table 12-2.
Number of Participants with Missing Data for, or Excluded from, the Psychological Assessment

		Group		Dioxin (Ranch Hands Only)		Categorized Dioxin	
Variable	Variable Use	Ranch Hand	Comparison	Initial	Current	Ranch Hand	Comparison
12 SCL-90-R T-Scores	DEP	1	1	1	1	1	1
Current Alcohol Use	COV	10	18	7	9	9	16
Lifetime Alcohol History	COV	22	21	13	20	20	18
Current Total Household Income	COV	11	18	4	11	11	15
Current Employment	COV	0	2	0	0	0	2
Current Marital Status	COV	0	2	0	0	0	0
Pre-SEA Alcohol Dependence	EXC	0	1	0	0	0	0
Pre-SEA Anxiety	EXC	5	3	2	4	4	3
Pre-SEA Other Neuroses	EXC	13	12	6	13	13	11
HIV Positive	EXC	3	1	2	3	3	1

Abbreviations: DEP = Dependent variable (missing data).
COV = Covariate (missing data).
EXC = Exclusion.

Note: 952 Ranch Hands and 1,281 Comparisons;
520 Ranch Hands for initial dioxin; 894 Ranch Hands for current dioxin;
894 Ranch Hands and 1,063 Comparisons for categorized dioxin.
One Ranch Hand missing total lipids for current dioxin.

The anxiety variable was significantly associated with age, indicating younger participants had a higher history of anxiety ($p=0.041$). Occupation also was significantly associated with anxiety ($p<0.001$), with the highest history of anxiety among enlisted groundcrew, followed by enlisted flyers and then officers. Additionally, education level and current total household income each demonstrated a significant inverse association with anxiety ($p<0.001$ for both associations). Those participants only a high-school education and those with an income of less than or equal to $55,000 had a higher incidence of anxiety. Participants who were currently unmarried at the time of the examination exhibited a significantly higher history of anxiety than participants who were currently married ($p=0.001$).

Tests for the other neuroses variable revealed several highly significant associations. Among the occupational strata, enlisted flyers exhibited the most history of other neuroses ($p<0.001$). Also, a significant association between other neuroses and lifetime alcohol history was found ($p<0.001$). The history of other neuroses increased as the number of drink-years increased. Significantly higher histories of other neuroses were found for the high-school-educated participants, those with a current total household income less than or equal to $55,000, those not currently employed, and participants not currently married ($p<0.001$, $p<0.001$, $p=0.040$, and $p<0.001$ respectively).

SCL-90-R anxiety and SCL-90-R depression scores displayed similar association test results. Enlisted groundcrew exhibited the greatest percentage of high SCL-90-R anxiety T-scores and enlisted flyers exhibited the greatest percentage of high SCL-90-R depression T-scores ($p<0.001$ for each of the associations with occupation). The greatest percentage of high T-scores for both SCL-90-R anxiety and SCL-90-R depression were among participants in the greater than 40 drink-years category ($p=0.005$ and $p=0.003$ respectively for associations with lifetime alcohol history). The 0 drink-years category was next highest for both variables, followed by the greater than 0 to 40 drink-years category. Both scores were highest for the high-school-educated participants ($p<0.001$ for each score), participants with a current total household income less than or equal to $55,000 ($p<0.001$ for each), those not currently employed ($p=0.010$ and $p=0.001$ respectively), and participants not currently married ($p=0.002$ and $p<0.001$ respectively).

The SCL-90-R hostility score and occupation were found to be significantly associated with the largest percentage of high T-scores among the enlisted flyers ($p<0.001$). The association with lifetime alcohol history was also significant ($p=0.020$). The percentage of high T-scores increased as the number of drink-years increased. Significant associations also were found with each of education and current total household income ($p<0.001$ and $p=0.001$ respectively). T-scores were highest for the high-school-educated participants and those with a current total household income less than or equal to $55,000.

The percentages of SCL-90-R interpersonal sensitivity T-scores decreased with age ($p=0.009$) and occupation ($p<0.001$; enlisted groundcrew exhibited the highest percentage). Participants whose highest education level was high school, participants whose current total household income was less than or equal to $55,000, and participants who were not currently married each displayed the larger percentages of high SCL-90-R interpersonal sensitivity T-scores ($p<0.001$, $p<0.001$, and $p=0.001$ respectively).

Examination of SCL-90-R obsessive-compulsive behavior revealed a significant association with occupation ($p<0.001$), with the greatest percentage of high T-scores among the enlisted flyers. Lifetime alcohol history also was associated with obsessive-compulsive behavior, with the largest percentage among participants with more than 40 drink-years ($p=0.003$). Similar to other SCL-90-R measurements, the larger percentage of high obsessive-compulsive T-scores were for the high-school-educated participants ($p<0.001$), participants with a current total household income less than or equal to $55,000 ($p<0.001$), and those not currently employed ($p=0.003$).

The percentage of high SCL-90-R paranoid ideation T-scores was greater for Blacks than non-Blacks and higher for enlisted groundcrew and enlisted flyers than for officers ($p=0.016$ and $p<0.001$ respectively). As the number of lifetime drink-years of alcohol increased, the percentage of high T-scores also increased ($p=0.017$). Larger percentages of high T-scores were found among participants who were high-school educated only ($p<0.001$) and among participants with a current total household income less than or equal to $55,000 ($p<0.001$). Participants not currently married also displayed the higher percentage of high T-scores ($p=0.005$).

Several covariates demonstrated a significant association with SCL-90-R phobic anxiety. Occupation was significantly associated ($p<0.001$) and percentages of high T-scores increased from officers to enlisted flyers to enlisted groundcrew. The association with current alcohol use was also significant, with the heaviest current drinkers (greater than 4 drinks per day) having the largest percentage of high T-scores ($p=0.010$). The lifetime alcohol history association also was significant and displayed the greatest percentage of high T-scores among participants in the 0 drink-years stratum ($p=0.017$). Significantly higher percentages of high T-scores also were found for the high-school-educated participants, participants with a current total household income less than or equal to $55,000, those not currently employed, and those not currently married ($p<0.001$ for education, current total household income, and current employment; $p=0.009$ for current marital status).

Tests of association involving SCL-90-R psychoticism revealed significantly more Blacks than non-Blacks had a higher T-score ($p=0.042$), and percentages of high T-scores increased from officers to enlisted flyers to enlisted groundcrew ($p<0.001$). The lifetime alcohol history association also was significant ($p=0.005$). Participants in the greater than 40 drink-years category displayed the largest percentage of high T-scores. Greater percentages of high T-scores were found for high-school-educated participants and among those with a current total household income less than or equal to $55,000 ($p<0.001$ for both tests). Participants indicating that they were not currently employed, and those not currently married also displayed the larger percentage of high T-scores ($p=0.001$ and $p=0.004$ respectively).

SCL-90-R somatization was significantly associated with occupation ($p<0.001$), education ($p<0.001$), current total household income ($p<0.001$), current employment ($p=0.001$), and current marital status ($p<0.001$). Results were similar to the results observed for SCL-90-R psychoticism.

Results of association tests involving SCL-90-R global severity index and SCL-90-R positive symptom total were similar. Enlisted groundcrew and those participants with more than 40 lifetime drink-years of alcohol exhibited the greatest percentage of high T-scores for both variables ($p \leq 0.001$ for each test). Patterns of percentages of high T-scores for both variables for education, current total household income, current employment, and current marital status are similar in direction and significance to patterns for SCL-90-R psychoticism ($p<0.001$ for education, current total household income, and current marital status; $p=0.006$ and $p=0.005$ respectively, for the associations between current employment and the SCL-90-R global severity index and SCL-90-R positive symptom total).

Occupation, current alcohol use, education, and current total household income were significantly associated with the SCL-90-R positive symptom distress index. The enlisted flyer stratum and the greater than 4 drinks per day stratum of current alcohol use demonstrated the largest percentages of high T-scores ($p<0.001$ and $p=0.017$ respectively). The high-school-educated participants exhibited a larger percentage of high T-scores than college graduates ($p=0.004$), and participants with a current total household income less than or equal to $55,000 displayed a higher percentage of high T-scores than participants in the greater than $55,000 category ($p<0.001$).

In summary, few variables were significantly associated with age, race, and current alcohol use, while most variables were associated with occupation, lifetime alcohol history, education, current total household income, current employment, and current marital status. No variables were found significantly associated with current parental status or combat service.

Exposure Analysis

The following section presents results of the statistical analyses of the dependent variables shown in Table 12-1. Dependent variables are grouped into two sections: those derived and verified from a review of medical records and data obtained during the 1992 psychological examination.

Unadjusted and adjusted analyses of six models are presented for each variable. Model 1 examines the relationship between the dependent variable and group (Ranch Hand or Comparison). Model 2 explores the relationship between the dependent variable and an extrapolated initial dioxin measure for Ranch Hands who had a 1987 dioxin measurement greater than 10 ppt. If a participant did not have a 1987 dioxin level, a 1992 level was used. A statistical adjustment for the percent of body fat at the participant's time of duty in SEA and the change in the percent of body fat from the time of duty in SEA to the date of the blood draw for dioxin is included in this model to account for body-fat-related difference in elimination rate (37). Model 3 dichotomizes the Ranch Hands in Model 2 based on their initial dioxin measures; these two categories of Ranch Hands are referred to as the "low Ranch Hand" category and the "high Ranch Hand" category. These participants are added to Ranch Hands and Comparisons with current serum dioxin levels (1987, if available; 1992, if the 1987 level was not available) at or below 10 ppt to create a total of four categories. Ranch Hands with current serum dioxin levels at or below 10 ppt are referred to as the "background Ranch Hand" category. The relationship between the dependent variable in

each of the three Ranch Hand categories and the dependent variable in the "Comparison" category is examined. A fourth contrast, exploring the relationship of the dependent variable in the low Ranch Hand category and the high Ranch Hand category combined, also is conducted. This combination is referred to in the text and tables as the "low plus high Ranch Hand" category. As in Model 2, a statistical adjustment is made for the percent of body fat at the participant's time of duty in SEA and the change in the percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

Models 4, 5, and 6 examine the relationship between the dependent variable and 1987 dioxin levels in all Ranch Hands with a dioxin measurement. If a participant did not have a 1987 dioxin measurement, a 1992 measurement was utilized in determining the current dioxin level. The measure of dioxin in Model 4 is lipid-adjusted, whereas whole-weight dioxin is used in Models 5 and 6. Model 6 differs from Model 5 in that a statistical adjustment for total lipids is included in Model 6. Details on dioxin and the modeling strategy are found in Chapters 2 and 7 respectively.

Results of investigations for group-by-covariate and dioxin-by-covariate interactions are referenced in the text, and tabular results are presented in Appendix H-2. As described previously, additional analyses are performed when occupation was retained in the final models for Models 2 through 6. Results excluding occupation from these models are shown in Appendix H-3, and dioxin-by-covariate interactions with occupation excluded from these models are presented in Appendix H-4. Results from analyses excluding occupation are discussed in the text only if a meaningful change in the results occurred (that is, changes between significant results, marginally significant results, and nonsignificant results).

Verified Medical Records Variables

Psychoses

All unadjusted and adjusted analyses of a history of psychoses for Models 1-6 were nonsignificant (Table 12-3(a-f): $p>0.24$ for all analyses). Current total household income and current marital status were significant covariates for each adjusted model. Model 1 also adjusted for the effects of race and lifetime alcohol history. Combat service was additionally significant for Models 2, 4, 5, and 6.

Alcohol Dependence

Results from the Model 1 unadjusted and adjusted analyses of a history of alcohol dependence were nonsignificant (Table 12-4(a,b): $p>0.25$ for each contrast). Adjusted results were based on the final model after deletion of the significant group-by-current marital status interaction. Current total household income and current parental status also were significant in the final adjusted model. Appendix Table H-2-1 presents results stratified by current marital status.

Table 12-3.
Analysis of Psychoses

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Yes**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***949***	***2.9***	***0.98 (0.60,1.63)***	***0.999***
	Comparison	***1,280***	***2.9***		
Officer	Ranch Hand	367	1.9	0.96 (0.36,2.53)	0.999
	Comparison	501	2.0		
Enlisted Flyer	Ranch Hand	162	4.3	2.25 (0.65,7.81)	0.319
	Comparison	203	2.0		
Enlisted Groundcrew	Ranch Hand	420	3.1	0.77 (0.38,1.53)	0.563
	Comparison	576	4.0		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.04 (0.62,1.73)***	***0.888***	RACE (p=0.105) DRKYR (p=0.076) INC (p=0.009) MARITAL (p<0.001)
Officer	1.10 (0.40,3.01)	0.849	
Enlisted Flyer	2.10 (0.60,7.41)	0.247	
Enlisted Groundcrew	0.80 (0.40,1.63)	0.545	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 12-3. (Continued)
Analysis of Psychoses

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	174	5.2	0.91 (0.62,1.33)	0.604
Medium	173	1.2		
High	171	4.1		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
514	0.81 (0.54,1.22)	0.302	INC (p=0.090) MARITAL (p=0.009) COMBDAYS (p=0.126)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 12-3. (Continued)
Analysis of Psychoses

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,062	3.0		
Background RH	373	1.9	0.67 (0.29,1.53)	0.336
Low RH	260	3.5	1.13 (0.53,2.42)	0.745
High RH	258	3.5	1.07 (0.50,2.28)	0.867
Low plus High RH	518	3.5	1.10 (0.61,1.99)	0.753

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,047			INC ($p=0.097$) MARITAL ($p<0.001$)
Background RH	366	0.76 (0.33,1.77)	0.525	
Low RH	256	1.21 (0.56,2.58)	0.631	
High RH	258	0.95 (0.44,2.06)	0.897	
Low plus High RH	514	1.07 (0.59,1.94)	0.834	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 12-3. (Continued)
Analysis of Psychoses

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Yes/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	2.0 (294)	3.3 (300)	3.0 (297)	1.10 (0.84,1.43)	0.495
5	1.7 (299)	3.7 (297)	3.1 (295)	1.13 (0.89,1.42)	0.324
6[c]	1.7 (298)	3.7 (297)	3.1 (295)	1.06 (0.82,1.37)	0.650

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	880	1.00 (0.76,1.32)	0.983	INC (p=0.041) MARITAL (p=0.001) COMBDAYS (p=0.113)
5	880	1.04 (0.82,1.32)	0.749	INC (p=0.048) MARITAL (p<0.001) COMBDAYS (p=0.122)
6[d]	879	0.98 (0.76,1.27)	0.881	INC (p=0.052) MARITAL (p=0.001) COMBDAYS (p=0.107)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for $\log_2$ total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for $\log_2$ total lipids.

[d] Adjusted for $\log_2$ total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 12-4.
Analysis of Alcohol Dependence

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Yes**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***949***	***7.5***	***1.15 (0.83,1.60)***	***0.451***
	Comparison	***1,279***	***6.6***		
Officer	Ranch Hand	367	4.6	0.89 (0.47,1.66)	0.829
	Comparison	501	5.2		
Enlisted Flyer	Ranch Hand	162	9.9	1.20 (0.59,2.45)	0.754
	Comparison	203	8.4		
Enlisted Groundcrew	Ranch Hand	420	9.1	1.30 (0.82,2.05)	0.324
	Comparison	575	7.1		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.17 (0.84,1.64)*****	***0.355*****	GROUP*MARITAL (p=0.026) INC (p<0.001) PARENT (p=0.080)
Officer	0.92 (0.49,1.73)**	0.789**	
Enlisted Flyer	1.21 (0.58,2.53)**	0.621**	
Enlisted Groundcrew	1.32 (0.82,2.12)**	0.256**	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

** Group-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table H-2-1 for further analysis of this interaction.

Table 12-4. (Continued)
Analysis of Alcohol Dependence

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	174	8.6	1.05 (0.81,1.35)	0.722
Medium	173	4.6		
High	171	9.4		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
514	1.06 (0.81,1.40)	0.666	RACE (p=0.096) INC (p=0.016) PARENT (p=0.071)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 12-4. (Continued)
Analysis of Alcohol Dependence

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,062	6.4		
Background RH	373	7.5	1.18 (0.74,1.87)	0.484
Low RH	260	7.7	1.21 (0.72,2.03)	0.475
High RH	258	7.4	1.17 (0.69,1.99)	0.557
Low plus High RH	518	7.5	1.19 (0.79,1.79)	0.404

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,047			INC ($p<0.001$) MARITAL ($p<0.001$) PARENT ($p=0.030$)
Background RH	366	1.34 (0.83,2.16)	0.227	
Low RH	256	1.16 (0.67,1.98)	0.599	
High RH	258	1.04 (0.61,1.80)	0.879	
Low plus High RH	514	1.10 (0.72,1.67)	0.666	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 12-4. (Continued)
Analysis of Alcohol Dependence

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Yes/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	6.8 (294)	8.3 (300)	7.4 (297)	0.98 (0.83,1.17)	0.851
5	7.4 (299)	7.4 (297)	7.8 (295)	0.99 (0.85,1.14)	0.865
6[c]	7.4 (298)	7.4 (297)	7.8 (295)	0.95 (0.81,1.11)	0.511

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	880	0.86 (0.72,1.03)	0.097	EDUC (p=0.108) INC (p<0.001) COMBDAYS (p=0.059)
5	880	0.89 (0.77,1.03)	0.122	EDUC (p=0.115) INC (p<0.001) COMBDAYS (p=0.062)
6[d]	879	0.84 (0.72,0.99)	0.036	EDUC (p=0.102) INC (p<0.001) COMBDAYS (p=0.053)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Analysis of associations between a history of alcohol dependence and dioxin in Models 2 and 3 showed nonsignificant results (Table 12-4(c-f): $p>0.22$ for all analyses). Current total household income and current parental status were each significant in both adjusted models. Model 2 also reflects the covariate effect of race and Model 3 additionally adjusted for current marital status.

Results were nonsignificant from the unadjusted analyses of a history of alcohol dependence for Models 4, 5, and 6 (Table 12-4(g): $p>0.51$ for each analysis). After covariate adjustment, Model 4 displayed marginally significant results, while Model 6 showed a significant relationship (Table 12-4(h): $p=0.097$, Adj. RR=0.86; and $p=0.036$, Adj. RR=0.84 for Models 4 and 6 respectively). Model 5 remained nonsignificant after adjustment (Table 12-4(h): $p=0.122$). Adjusted analyses of Models 4 and 6 revealed that a history of alcohol dependence decreased as current dioxin levels increased. Each model adjusted for education, current total household income, and combat service.

Drug Dependence

Due to the sparse history of drug dependence among study participants, only selected analyses were possible and are discussed below. Only one Comparison and four Ranch Hands had a verified history of drug dependence.

Model 1 analyses of drug dependence contrasting Ranch Hands and Comparisons over all occupations and the within the enlisted groundcrew strata were nonsignificant for both the unadjusted and adjusted analyses (Table 12-5(a,b): $p>0.31$ for each contrast). Age and current total household income were significant covariates. Differences between background Ranch Hands and Comparisons also were nonsignificant from Model 3 analysis (Table 12-5(e,f): $p>0.68$ for both unadjusted and adjusted contrasts). Covariate adjustment included current total household income and current parental status. Only unadjusted analyses were possible for Models 4, 5, and 6 and each result was nonsignificant (Table 12-5(g): $p>0.17$).

Anxiety

Model 1 contrasts examining differences of a history of anxiety between Ranch Hands and Comparisons were nonsignificant for the unadjusted and adjusted analyses (Table 12-6(a,b): $p>0.49$ for each contrast). Race, occupation, current total household income, and current marital status displayed significant covariate effects in the final model.

Both Model 2 analyses were nonsignificant (Table 12-6(c,d): $p>0.13$ for each analysis). Adjusted results were based on the final model after the deletion of the significant interaction between initial dioxin and occupation. Age, race, and current employment also were significant in the final model. Results stratified by occupation are presented in Appendix Table H-2-2.

The difference between high Ranch Hands and Comparisons was significant in the unadjusted analysis of Model 3 (Table 12-6(e): $p=0.044$, Est. RR=1.43), but was nonsignificant in the adjusted analysis (Table 12-6(f): $p=0.915$). All other Model 3

Table 12-5.
Analysis of Drug Dependence

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	Group	n	Percent Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***949***	***0.1***	***0.34 (0.04,3.02)***	***0.569***
	Comparison	***1,280***	***0.3***		
Officer	Ranch Hand	367	0.0	--	--
	Comparison	501	0.2		
Enlisted Flyer	Ranch Hand	162	0.0	--	--
	Comparison	203	0.0		
Enlisted Groundcrew	Ranch Hand	420	0.2	0.46 (0.05,4.40)	0.850
	Comparison	576	0.5		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	***0.36 (0.04,3.23)***	***0.317***	AGE (p=0.023) INC (p=0.022)
Officer	--	--	
Enlisted Flyer	--	--	
Enlisted Groundcrew	0.49 (0.05,4.84)	0.517	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

--: Relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities.

Table 12-5. (Continued)
Analysis of Drug Dependence

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	174	0.0	--	--
Medium	173	0.0		
High	171	0.0		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
--	--	--	

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

--: Analysis not performed due to the sparse number of abnormalities.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 12-5. (Continued)
Analysis of Drug Dependence

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,062	0.3		
Background RH	373	0.3	0.62 (0.06,6.22)	0.684
Low RH	260	0.0	--	--
High RH	258	0.0	--	--
Low plus High RH	518	0.0	--	--

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,047			INC (p=0.015) PARENT (p=0.046)
Background RH	366	1.21 (0.11,13.45)	0.787	
Low RH	256	--	--	
High RH	258	--	--	
Low plus High RH	514	--	--	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

--: Relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 12-5. (Continued)
Analysis of Drug Dependence

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Yes/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	0.3 (294)	0.0 (300)	0.0 (297)	0.36 (0.08,1.54)	0.176
5	0.3 (299)	0.0 (297)	0.0 (295)	0.55 (0.25,1.21)	0.202
6[c]	0.3 (298)	0.0 (297)	0.0 (295)	0.58 (0.23,1.47)	0.320

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	--	--	--	
5	--	--	--	
6[c]	--	--	--	

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

--: Analyses not performed due to the sparse number of abnormalities.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 12-6.
Analysis of Anxiety

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Yes**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***944***	***14.8***	***1.06 (0.84,1.35)***	***0.670***
	Comparison	***1,277***	***14.1***		
Officer	Ranch Hand	366	6.8	1.08 (0.63,1.85)	0.903
	Comparison	501	6.4		
Enlisted Flyer	Ranch Hand	161	16.8	1.00 (0.58,1.74)	0.999
	Comparison	203	16.8		
Enlisted Groundcrew	Ranch Hand	417	21.1	1.08 (0.79,1.47)	0.700
	Comparison	573	19.9		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.09 (0.85,1.39)***	***0.499***	RACE (p=0.035)
Officer	1.07 (0.62,1.85)	0.809	OCC (p<0.001)
Enlisted Flyer	1.04 (0.59,1.82)	0.899	INC (p<0.001)
Enlisted Groundcrew	1.11 (0.81,1.52)	0.506	MARITAL (p=0.045)

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 12-6. (Continued)
Analysis of Anxiety

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	173	12.1	1.14 (0.96,1.35)	0.139
Medium	173	19.1		
High	170	18.2		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
516	0.94 (0.77,1.16)**	0.574**	INIT*OCC (p=0.037) AGE (p=0.028) RACE (p=0.037) EMPLOY (p=0.001)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table H-2-2 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.
INIT = Log_2 (initial dioxin).

Table 12-6. (Continued)
Analysis of Anxiety

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,059	14.8		
Background RH	371	13.5	0.91 (0.64,1.28)	0.585
Low RH	259	12.7	0.84 (0.56,1.26)	0.395
High RH	257	20.2	1.43 (1.01,2.04)	0.044
Low plus High RH	516	16.5	1.12 (0.84,1.50)	0.433

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,044			RACE (p=0.055) OCC (p<0.001) INC (p=0.005) MARITAL (p=0.037)
Background RH	364	1.27 (0.88,1.84)	0.203	
Low RH	255	0.91 (0.60,1.37)	0.639	
High RH	257	1.02 (0.71,1.46)	0.915	
Low plus High RH	512	0.97 (0.72,1.31)	0.840	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 12-6. (Continued)
Analysis of Anxiety

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Yes/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	14.0 (292)	12.4 (299)	19.3 (296)	1.13 (1.00,1.28)	0.056
5	13.5 (297)	13.2 (296)	19.1 (294)	1.12 (1.00,1.25)	0.041
6[c]	13.5 (296)	13.2 (296)	19.1 (294)	1.09 (0.97,1.22)	0.154

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	887	0.94 (0.82,1.07)	0.343	RACE (p=0.010) OCC (p<0.001) EMPLOY (p=0.022) MARITAL (p=0.069)
5	887	0.96 (0.85,1.08)	0.495	RACE (p=0.011) OCC (p<0.001) EMPLOY (p=0.021) MARITAL (p=0.069)
6[d]	886	0.92 (0.81,1.04)	0.197	RACE (p=0.015) OCC (p<0.001) EMPLOY (p=0.021) MARITAL (p=0.081)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

contrasts were nonsignificant (Table 12-6(e,f): $p>0.20$ for all remaining contrasts). Significant covariates in the adjusted analysis included race, occupation, current total household income, and current marital status.

The Model 4 unadjusted analysis of anxiety revealed a marginally significant association between current dioxin and history of anxiety (Table 12-6(g): $p=0.056$, Est. RR=1.13). Results were significant from the Model 5 unadjusted analysis (Table 12-6(g): $p=0.041$, Est. RR=1.12). Both analyses suggest that the greater percentage of those reporting a history of anxiety among Ranch Hands were those with the highest levels of current dioxin. The test of association was nonsignificant for the Model 6 unadjusted analysis as well for the adjusted analysis for each of Models 4, 5, and 6 (Table 12-6(g,h): $p>0.15$ for all remaining analyses). Each model adjusted for the covariate effects of race, occupation, current employment, and current marital status. After exclusion of occupation from Models 4 and 5, results became significant (Appendix Table H-3-1(c): $p=0.037$, Adj. RR=1.14; and $p=0.029$, Adj. RR=1.13). However, education was not included in this auxiliary analysis. When education was added to the final model, the results of the analysis for Models 4, 5,and 6 were nonsignificant (Appendix Table H-3-2(a): $p=0.276$, $p=0.219$, and $p=0.494$ for Models 4, 5, and 6 respectively).

Other Neuroses

Analysis of a history of other neuroses revealed significant differences between Ranch Hands and Comparisons from Model 1. The enlisted groundcrew unadjusted and adjusted contrasts were significant, with 47.6 percent of Ranch Hands and 40.8 percent of Comparisons having a history of other neuroses (Table 12-7(a,b): $p=0.040$, Est. RR=1.32; and $p=0.017$, Adj. RR=1.39, for the unadjusted and adjusted analyses). The adjusted contrast combining all occupations was significant also (Table 12-7(b): $p=0.034$, Adj. RR=1.22). All remaining contrasts were nonsignificant (Table 12-7(a,b): $p>0.10$ for all remaining contrasts). Adjusted results are based on the final model after deletion of the significant interactions between group and education and between group and current total household income. Results presented for each level of education and current total household income are found in Appendix Table H-2-3. Age, occupation, lifetime alcohol history, current marital status, and current parental status were significant covariates in the adjusted model.

The Model 2 analysis of a history of other neuroses exhibited nonsignificant results for both the unadjusted and adjusted models (Table 12-7(c,d): $p>0.51$ for both analyses). Covariates included in the final model were lifetime alcohol history, education, current employment, current marital status, and current parental status.

Unadjusted contrasts with Comparisons in Model 3 displayed a nonsignificant difference with background Ranch Hands, a marginally significant difference with low Ranch Hands, and significant differences with high Ranch Hands and with low plus high Ranch Hands (Table 12-7(e): $p=0.293$ for background Ranch Hands versus Comparisons; $p=0.056$, Est. RR=1.31 for low Ranch Hands versus Comparisons; $p=0.037$, Est. RR=1.34 for high Ranch Hands versus Comparisons; and $p=0.010$, Est. RR=1.33 for low plus high Ranch

Table 12-7.
Analysis of Other Neuroses

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Yes**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***936***	***40.3***	***1.16 (0.98,1.38)***	***0.101***
	Comparison	***1,268***	***36.8***		
Officer	Ranch Hand	364	28.6	0.96 (0.71,1.29)	0.836
	Comparison	499	29.5		
Enlisted Flyer	Ranch Hand	160	48.1	1.21 (0.79,1.83)	0.442
	Comparison	200	43.5		
Enlisted Groundcrew	Ranch Hand	412	47.6	1.32 (1.02,1.70)	0.040
	Comparison	569	40.8		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.22 (1.02,1.47)****	***0.034****	GROUP*EDUC (p<0.001) GROUP*INC (p=0.032)
Officer	1.00 (0.73,1.36)**	0.999**	AGE (p=0.052) OCC (p<0.001)
Enlisted Flyer	1.30 (0.84,2.01)**	0.242**	DRKYR (p<0.001) MARITAL (p<0.001)
Enlisted Groundcrew	1.39 (1.06,1.81)**	0.017**	PARENT (p=0.028)

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

** Group-by-covariate interactions ($p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table H-2-3 for further analysis of these interactions.

Table 12-7. (Continued)
Analysis of Other Neuroses

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	172	42.4	1.04 (0.92,1.19)	0.518
Medium	171	48.0		
High	169	45.6		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
499	1.03 (0.89,1.19)	0.714	DRKYR (p=0.009) EDUC (p=0.002) EMPLOY (p=0.035) MARITAL (p=0.007) PARENT (p=0.077)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 12-7. (Continued)
Analysis of Other Neuroses

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	**n**	**Percent Yes**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,051	38.3		
Background RH	366	34.7	0.87 (0.68,1.12)	0.293
Low RH	257	44.8	1.31 (0.99,1.73)	0.056
High RH	255	45.9	1.34 (1.02,1.77)	0.037
Low plus High RH	512	45.3	1.33 (1.07,1.64)	0.010

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	**n**	**Adj. Relative Risk (95% C.I.)[ac]**	**p-Value**	**Covariate Remarks**
Comparison	1,022			DXCAT*DRKYR (p=0.011) DXCAT*EDUC (p<0.001) DXCAT*INC (p=0.035) DXCAT*COMBDAYS (p=0.029) OCC (p<0.001) EMPLOY (p=0.038) MARITAL (p<0.001)
Background RH	352	1.09 (0.81,1.46)**	0.574**	
Low RH	247	1.27 (0.92,1.75)**	0.142**	
High RH	248	1.08 (0.78,1.51)**	0.630**	
Low plus High RH	495	1.18 (0.90,1.54)**	0.222**	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interaction ($p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table H-2-3 for further analysis of these interactions.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.
DXCAT = Categorized Dioxin.

Table 12-7. (Continued)
Analysis of Other Neuroses

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Yes/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	33.0 (288)	43.1 (297)	46.4 (293)	1.12 (1.02,1.23)	0.013
5	32.8 (293)	42.5 (294)	47.4 (291)	1.12 (1.03,1.21)	0.005
6[c]	32.5 (292)	42.5 (294)	47.4 (291)	1.07 (0.98,1.17)	0.139

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	858	0.98 (0.88,1.10)**	0.777**	CURR*DRKYR (p=0.038) OCC (p=0.026) EDUC (p=0.003) EMPLOY (p=0.029) MARITAL (p=0.002) PARENT (p=0.100)
5	858	1.01 (0.92,1.11)**	0.816**	CURR*DRKYR (p=0.013) OCC (p=0.043) EDUC (p=0.002) EMPLOY (p=0.027) MARITAL (p=0.002) PARENT (p=0.103)
6[d]	857	0.95 (0.85,1.05)**	0.301**	CURR*DRKYR (p=0.014) OCC (p=0.020) EDUC (p=0.004) EMPLOY (p=0.020) MARITAL (p=0.002) PARENT (p=0.068)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.
[c] Adjusted for log_2 total lipids.
[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table H-2-3 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.
CURR = Log_2 (current dioxin + 1).

Hands versus Comparisons). The analyses indicated that a history of other neuroses increased with dioxin. Adjusted contrasts were nonsignificant (Table 12-7(f): $p>0.14$ for each adjusted contrast). Adjusted results are based on the final model after the deletion of the significant categorized dioxin interactions with each of the following covariates: lifetime alcohol history, education, current total household income, and combat service. Appendix Table H-2-3 presents analysis stratified by each level the covariates involved in the interactions. Occupation, current employment, and current marital status also were significant in the final model. Exclusion of occupation from the final model changed nonsignificant results to marginally significant results for the high Ranch Hands and low plus high Ranch Hands contrasts (Appendix Table H-3-2(a): $p=0.093$, Adj. RR=1.25; and $p=0.063$, Adj. RR=1.28 respectively).

Significant relative risk estimates resulted from the unadjusted analyses of other neuroses for Models 4 and 5 (Table 12-7(g): $p=0.013$, Est. RR=1.12 and $p=0.005$, Est. RR=1.12). The percentage of Ranch Hands having a history of other neuroses increased as current dioxin levels increased. Results from the unadjusted Model 6 analysis and the adjusted Models 4, 5, and 6 analyses were each nonsignificant (Table 12-7(g,h): $p>0.13$ for each analysis). All adjusted results are based on each final model after the deletion of the significant current dioxin-by-lifetime alcohol history interaction. Results stratified by each category of lifetime alcohol history are presented in Appendix Table H-2-3. Occupation, education, current employment, current marital status, and current parental status were each additionally included as significant covariates in each final model.

Psychological Examination Variables

SCL-90-R Anxiety

Marginally significant differences in the prevalence of high SCL-90-R anxiety T-scores were found between Ranch Hands and Comparisons from the Model 1 unadjusted contrast combining all occupations (Table 12-8(a): $p=0.071$, Est. RR=1.38). Results became significant after covariate adjustment (Table 12-8(b): $p=0.039$, Adj. RR=1.44). Adjusted analysis also revealed a marginally significant difference within the enlisted flyer stratum (Table 12-8(b): $p=0.098$, Adj. RR=1.92). All other Model 1 contrasts were nonsignificant (Table 12-8(a,b): $p>0.21$ for all remaining contrasts). Significant covariates in the final adjusted model were occupation, lifetime alcohol history, current total household income, and current employment.

Associations between SCL-90-R anxiety and initial dioxin were nonsignificant for both the Model 2 unadjusted and adjusted analyses (Table 12-8(c,d): $p>0.33$ for both analyses). Significant covariate effects in the final adjusted model included lifetime alcohol history, education, current total household income, current marital status, and combat service. Initial dioxin-by-occupation and initial dioxin-by-current alcohol use interactions also were significant in the analysis. Adjusted results are based on the final model after deletion of the interactions. Results stratified by occupation and current alcohol use category are presented in Appendix Table H-2-4.

Table 12-8.
Analysis of SCL-90-R Anxiety

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	Group	n	Percent High	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***948***	***7.8***	***1.38 (0.99,1.93)***	***0.071***
	Comparison	***1,279***	***5.8***		
Officer	Ranch Hand	367	3.5	1.50 (0.68,3.32)	0.428
	Comparison	501	2.4		
Enlisted Flyer	Ranch Hand	161	11.2	1.70 (0.82,3.53)	0.212
	Comparison	203	6.9		
Enlisted Groundcrew	Ranch Hand	420	10.2	1.25 (0.81,1.93)	0.363
	Comparison	575	8.4		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	***1.44 (1.02,2.05)***	***0.039***	OCC (p=0.014) DRKYR (p=0.010) INC (p<0.001) EMPLOY (p=0.095)
Officer	1.62 (0.73,3.62)	0.238	
Enlisted Flyer	1.92 (0.89,4.16)	0.098	
Enlisted Groundcrew	1.26 (0.81,1.98)	0.306	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 12-8. (Continued)
Analysis of SCL-90-R Anxiety

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	173	7.5	1.11 (0.90,1.39)	0.335
Medium	173	9.3		
High	171	11.1		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
500	1.04 (0.81,1.35)**	0.740**	INIT*OCC (p=0.031) INIT*ALC (p=0.029) DRKYR (p=0.018) EDUC (p=0.127) INC (p=0.005) MARITAL (p=0.069) COMBDAYS (p=0.140)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interactions ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table H-2-4 for further analysis of these interactions.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 12-8. (Continued)
Analysis of SCL-90-R Anxiety

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,061	5.6		
Background RH	373	5.1	0.94 (0.55,1.60)	0.812
Low RH	259	7.3	1.32 (0.77,2.26)	0.309
High RH	258	11.2	2.11 (1.32,3.38)	0.002
Low plus High RH	517	9.3	1.71 (1.14,2.54)	0.009

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,031			OCC (p=0.022) DRKYR (p=0.012) INC (p<0.001) EMPLOY (p=0.089)
Background RH	359	1.33 (0.76,2.34)	0.318	
Low RH	249	1.30 (0.73,2.31)	0.373	
High RH	251	1.67 (1.02,2.73)	0.041	
Low plus High RH	500	1.50 (0.99,2.29)	0.056	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 12-8. (Continued)
Analysis of SCL-90-R Anxiety

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent High/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	4.8 (294)	7.0 (299)	10.8 (297)	1.26 (1.07,1.49)	0.005
5	4.4 (299)	8.1 (296)	10.2 (295)	1.26 (1.09,1.46)	0.002
6[c]	4.4 (298)	8.1 (296)	10.2 (295)	1.22 (1.04,1.43)	0.013

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	859	1.13 (0.96,1.34)**	0.146**	CURR*ALC (p=0.022) DRKYR (p=0.018) EDUC (p=0.040) INC (p=0.004)
5	859	1.15 (0.99,1.34)**	0.069**	CURR*ALC (p=0.036) DRKYR (p=0.021) EDUC (p=0.046) INC (p=0.004)
6[d]	858	1.10 (0.94,1.30)**	0.240**	CURR*ALC (p=0.039) DRKYR (p=0.023) EDUC (p=0.046) INC (p=0.003)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table H-2-4 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Significant Model 3 results were found from the unadjusted and adjusted analysis of SCL-90-R anxiety contrasting high Ranch Hands and Comparisons (Table 12-8(e,f): $p=0.002$, Est. RR=2.11 and $p=0.041$, Adj. RR=1.67 respectively). The unadjusted low plus high Ranch Hand contrast also was significant but became marginally significant after covariate adjustment (Table 12-8(e,f): $p=0.009$, Est. RR=1.71 and $p=0.056$, Adj. RR=1.50 for the unadjusted and adjusted analyses). Occupation, lifetime alcohol history, current total household income, and current employment were significant in the final adjusted model. However, after exclusion of occupation from the final model, the low plus high Ranch Hands contrast became significant (Appendix Table H-3-4(b): $p=0.022$, Adj. RR=1.62). Other Model 3 contrasts were nonsignificant (Table 12-8(e,f): $p>0.30$ for all remaining contrasts).

Models 4, 5, and 6 each displayed a significant association between SCL-90-R anxiety and current dioxin in the unadjusted analysis (Table 12-8(g): $p=0.005$, Est. RR=1.26; $p=0.002$, Est. RR=1.26; and $p=0.013$, Est. RR=1.22 respectively). The relative risk estimates that were greater than one indicate the prevalence of high SCL-90-R anxiety T-scores increased as current dioxin levels increased. The Model 5 association became marginally significant after covariate adjustment (Table 12-8(h): $p=0.069$, Adj. RR=1.15). Models 4 and 6 became nonsignificant after covariate adjustment (Table 12-8(h): $p>0.14$ for both analyses). All adjusted results are based on the final model after deletion of the significant current dioxin-by-current alcohol use interaction. Results stratified by each category of current alcohol use are presented in Appendix Table H-2-4. Other significant covariates present in the final model were lifetime alcohol history, education, and current total household income.

SCL-90-R Depression

All differences examined between Ranch Hands and Comparisons from the Model 1 unadjusted and adjusted analyses of SCL-90-R depression were nonsignificant (Table 12-9(a,b): $p>0.18$ for all contrasts). Lifetime alcohol history, education, current total household income, current employment, and current marital status were significant covariates in the final adjusted model.

Results from the Model 2 unadjusted analysis of SCL-90-R depression also were nonsignificant (Table 12-9(a): $p=0.148$). Adjusted analysis revealed a significant interaction between initial dioxin and lifetime alcohol history. Results stratified by each category of lifetime alcohol history are presented in Appendix Table H-2-5. After deleting the initial dioxin-by-lifetime alcohol history interaction, the adjusted analysis also showed a nonsignificant association between SCL-90-R depression and initial dioxin (Table 12-9(d): $p=0.115$). Education, current employment, and current marital status were other significant covariates in the final model.

The Model 3 unadjusted analysis revealed a significant difference between high Ranch Hands and Comparisons (Table 12-9(e): $p=0.031$, Est. RR=1.58), where 13.6 percent of high Ranch Hands and 8.8 percent of Comparisons exhibited a high SCL-90-R depression T-score. All other unadjusted and adjusted Model 3 contrasts indicated no significant differences (Table 12-9(e,f): $p>0.10$ for all remaining contrasts). Adjusted analysis

Table 12-9.
Analysis of SCL-90-R Depression

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	Group	n	Percent High	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***948***	***10.1***	***1.16 (0.87,1.55)***	***0.337***
	Comparison	***1,279***	***8.8***		
Officer	Ranch Hand	367	6.5	1.28 (0.72,2.27)	0.487
	Comparison	501	5.2		
Enlisted Flyer	Ranch Hand	161	14.9	1.37 (0.74,2.53)	0.393
	Comparison	203	11.3		
Enlisted Groundcrew	Ranch Hand	420	11.4	1.03 (0.69,1.53)	0.964
	Comparison	575	11.1		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	***1.21 (0.90,1.63)***	***0.210***	DRKYR (p=0.028) EDUC (p=0.003) INC (p=0.001) EMPLOY (p=0.030) MARITAL (p=0.001)
Officer	1.38 (0.77,2.47)	0.282	
Enlisted Flyer	1.55 (0.81,2.97)	0.184	
Enlisted Groundcrew	1.02 (0.67,1.55)	0.927	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 12-9. (Continued)
Analysis of SCL-90-R Depression

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	173	8.1	1.16 (0.95,1.42)	0.148
Medium	173	10.4		
High	171	13.5		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
504	1.20 (0.96,1.50)**	0.115**	INIT*DRKYR (p=0.001) EDUC (p=0.026) EMPLOY (p=0.066) MARITAL (p=0.003)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interaction ($p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table H-2-5 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 12-9. (Continued)
Analysis of SCL-90-R Depression

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,061	8.8		
Background RH	373	9.1	1.09 (0.72,1.65)	0.684
Low RH	259	7.7	0.85 (0.51,1.41)	0.527
High RH	258	13.6	1.58 (1.04,2.40)	0.031
Low plus High RH	517	10.6	1.20 (0.85,1.71)	0.303

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,031			ALC (p=0.129) DRKYR (p=0.010) EDUC (p=0.006) INC (p=0.021) EMPLOY (p=0.024) MARITAL (p<0.001)
Background RH	359	1.35 (0.87,2.09)	0.177	
Low RH	249	0.75 (0.43,1.30)	0.309	
High RH	251	1.43 (0.92,2.22)	0.108	
Low plus High RH	500	1.10 (0.75,1.59)	0.629	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 12-9. (Continued)
Analysis of SCL-90-R Depression

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent High/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	8.8 (294)	8.7 (299)	12.5 (297)	1.10 (0.95,1.27)	0.207
5	9.4 (299)	7.8 (296)	12.9 (295)	1.11 (0.97,1.26)	0.125
6[c]	9.4 (298)	7.8 (296)	12.9 (295)	1.04 (0.90,1.19)	0.613

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	859	1.00 (0.86,1.18)**	0.961**	CURR*INC (p=0.032) DRKYR (p=0.028) EDUC (p=0.047) EMPLOY (p=0.038) MARITAL (p=0.022)
5	859	1.02 (0.89,1.17)**	0.783**	CURR*RACE (p=0.028) CURR*INC (p=0.008) DRKYR (p=0.041) EDUC (p=0.057) EMPLOY (p=0.036) MARITAL (p=0.010)
6[d]	858	0.95 (0.82,1.10)**	0.507**	CURR*RACE (p=0.023) CURR*INC (p=0.010) DRKYR (p=0.053) EDUC (p=0.045) EMPLOY (p=0.043) MARITAL (p=0.016)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table H-2-5 for further analysis of these interactions.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

displayed the significant covariate effects of current alcohol use, lifetime alcohol history, education, current total household income, current employment, and current marital status.

All results from the unadjusted and adjusted analyses of SCL-90-R depression for Models 4, 5, and 6 were nonsignificant (Table 12-9(g,h): $p>0.12$ for each analysis). Adjusted results displayed in Table 12-9(h) are based on the final models of Models 4, 5, and 6 after deletion of significant interactions involving current dioxin. Model 4 results stratified by each level of current total household income are found in Appendix Table H-2-5, as are Model 5 and 6 results stratified by race and by current total household income. Covariates significant for each model were lifetime alcohol history, education, current employment, and current marital status.

SCL-90-R Hostility

The Model 1 unadjusted analysis of SCL-90-R hostility revealed a significant group difference from the contrast combining all occupations. Results indicated a greater percentage of high T-scores for Ranch Hands (6.1%) than for Comparisons (4.1%) (Table 12-10(a): $p=0.044$, Est. RR=1.51). After covariate adjustment, the overall contrast presented a marginally significant difference (Table 12-10(b): $p=0.078$, Adj. RR=1.43). The unadjusted contrast within the enlisted groundcrew stratum and the adjusted contrast within the enlisted flyer stratum also displayed marginally significant differences between Ranch Hands and Comparisons (Table 12-10(a,b): $p=0.064$, Est. RR=1.65 and $p=0.091$, Adj. RR=2.04 respectively). All other Model 1 contrasts were nonsignificant (Table 12-10(a,b): $p>0.10$ for each remaining contrast). Lifetime alcohol history, current total household income, the group-by-current alcohol use interaction, and the group-by-education interaction were significant in the final adjusted model. All adjusted results are based on the final model after deletion of the group-by-covariate interactions. Appendix Table H-2-6 presents contrasts stratified by current alcohol use and education.

Model 2 unadjusted analysis of SCL-90-R hostility displayed a marginally significant positive association between initial dioxin and a high SCL-90-R hostility T-score (Table 12-10(c): $p=0.067$, Est. RR=1.26). After covariate adjustment for age, lifetime alcohol history, education, and current marital status, the association was nonsignificant (Table 12-10(d): $p=0.310$).

Model 3 contrasts involving background Ranch Hands and low Ranch Hands with Comparisons were nonsignificant for both the unadjusted and adjusted analyses of SCL-90-R hostility (Table 12-10(e,f): $p>0.10$ for each contrast). The high and the low plus high Ranch Hand contrasts revealed significant differences in the unadjusted analyses (Table 12-10(e): $p=0.008$, Est. RR=2.04 and $p=0.032$, Est. RR=1.64 respectively). Unadjusted analysis revealed a greater tendency of a high SCL-90-R hostility T-score among Ranch Hands with higher dioxin levels than Comparisons. After covariate adjustment for occupation, current alcohol use, lifetime alcohol history, and current total household income, the high Ranch Hand contrast became marginally significant and the low plus high contrast became nonsignificant (Table 12-10(f): $p=0.093$, Adj. RR=1.60 and $p=0.194$ respectively). Exclusion of occupation from the final model shifted the significance of the high contrast from marginally significant to significant (Appendix Table H-3-4(a): $p=0.027$,

Table 12-10.
Analysis of SCL-90-R Hostility

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent High**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***948***	***6.1***	***1.51 (1.03,2.21)***	***0.044***
	Comparison	***1,279***	***4.1***		
Officer	Ranch Hand	367	1.6	0.68 (0.25,1.82)	0.592
	Comparison	501	2.4		
Enlisted Flyer	Ranch Hand	161	9.9	2.13 (0.94,4.83)	0.101
	Comparison	203	4.9		
Enlisted Groundcrew	Ranch Hand	420	8.6	1.65 (1.00,2.71)	0.064
	Comparison	575	5.4		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.43 (0.96,2.14)*****	***0.078*****	GROUP*ALC (p=0.047) GROUP*EDUC (p=0.047) DRKYR (p<0.001) INC (p=0.009) OCC (p=0.061)
Officer	0.64 (0.22,1.86)**	0.411**	
Enlisted Flyer	2.04 (0.89,4.67)**	0.091**	
Enlisted Groundcrew	1.53 (0.91,2.57)**	0.106**	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

** Group-by-covariate interactions ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table H-2-6 for further analysis of these interactions.

Table 12-10. (Continued)
Analysis of SCL-90-R Hostility

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	173	5.8	1.26 (0.99,1.60)	0.067
Medium	173	5.2		
High	171	10.5		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
504	1.16 (0.87,1.53)	0.310	AGE (p=0.073) DRKYR (p=0.002) EDUC (p=0.017) MARITAL (p=0.026)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 12-10. (Continued)
Analysis of SCL-90-R Hostility

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,061	4.2		
Background RH	373	4.8	1.26 (0.71,2.21)	0.429
Low RH	259	5.4	1.25 (0.67,2.32)	0.484
High RH	258	8.9	2.04 (1.21,3.46)	0.008
Low plus High RH	517	7.2	1.64 (1.05,2.58)	0.032

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,031			OCC (p=0.020) ALC (p=0.025) DRKYR (p<0.001) INC (p=0.027)
Background RH	359	1.64 (0.89,3.02)	0.109	
Low RH	249	1.07 (0.54,2.14)	0.843	
High RH	251	1.60 (0.93,2.78)	0.093	
Low plus High RH	500	1.37 (0.85,2.21)	0.194	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 12-10. (Continued)
Analysis of SCL-90-R Hostility

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent High/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	4.4 (294)	5.4 (299)	8.8 (297)	1.28 (1.07,1.53)	0.008
5	4.0 (299)	6.4 (296)	8.1 (295)	1.27 (1.08,1.49)	0.004
6[c]	4.0 (298)	6.4 (296)	8.1 (295)	1.23 (1.04,1.46)	0.019

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	870	1.08 (0.89,1.33)	0.431	AGE (p=0.071) OCC (p=0.074) DRKYR (p<0.001) EDUC (p=0.061) EMPLOY (p=0.095)
5	870	1.10 (0.92,1.32)	0.275	AGE (p=0.069) OCC (p=0.082) DRKYR (p<0.001) EDUC (p=0.062) EMPLOY (p=0.090)
6[d]	869	1.05 (0.86,1.27)	0.645	AGE (p=0.054) OCC (p=0.066) DRKYR (p<0.001) EDUC (p=0.076) EMPLOY (p=0.074)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for $\log_2$ total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for $\log_2$ total lipids.

[d] Adjusted for $\log_2$ total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Adj. RR=1.84). The low plus high contrast changed from nonsignificant to marginally significant (Appendix Table H-3-5(a): p=0.098, Adj. RR=1.49). However, education was not included in this auxiliary analysis. When education was added to the final model, the results of the contrast between low plus high Ranch Hands and Comparisons for the SCL-90-R hostility T-scores were nonsignificant (Table H-3-6(a): p=0.144).

Positive associations between high SCL-90-R hostility T-scores and current dioxin were significant in the unadjusted analysis of Models 4, 5, and 6 (Table 12-10(g): p=0.008, Est. RR=1.28; p=0.004, Est. RR=1.27; and p=0.019, Est. RR=1.23, respectively). However, adjusted analyses were nonsignificant for each model (Table 12-10(h): p>0.27 for each analysis). Age, occupation, lifetime alcohol history, education, and current employment were significant in each final adjusted model.

SCL-90-R Interpersonal Sensitivity

Unadjusted and adjusted contrasts between Ranch Hands and Comparisons were each nonsignificant from the Model 1 analysis of SCL-90-R interpersonal sensitivity (Table 12-11(a,b): p>0.22 for each contrast). Occupation, lifetime alcohol history, education, and current total household income were each significant in the final adjusted model.

Results from the Model 2 analysis of SCL-90-R interpersonal sensitivity also were nonsignificant for both the unadjusted and adjusted analyses (Table 12-11(c,d): p>0.38 for both analyses). Adjusted results are based on the final model after deletion of the significant interactions of initial dioxin with occupation and lifetime alcohol history. Appendix Table H-2-7 presents analysis stratified by each category of occupation and lifetime alcohol history. Education, current total household income, current marital status, and current parental status were significant covariates in the final adjusted model.

The unadjusted analysis of Model 3 identified significantly more high Ranch Hands than Comparisons with a high SCL-90-R interpersonal sensitivity T-score (Table 12-11(e): p=0.024, Est. RR=1.62). Also, results were marginally significant for the unadjusted low plus high Ranch Hands contrast (Table 12-11(e): p=0.083, Est. RR=1.36). All remaining unadjusted contrasts and all adjusted contrasts were nonsignificant (Table 12-11(e,f): p>0.23 for all remaining contrasts). Occupation, lifetime alcohol history, current total household income, and current marital status were significant covariates in the final adjusted model. Exclusion of occupation from the adjusted model revealed a marginally significant difference between high Ranch Hands and Comparisons (Appendix Table H-3-5(b): p=0.075, Adj. RR=1.48). However, education was not included in this auxiliary analysis. When education was added to the final model, the results of the contrast between high Ranch Hands and Comparisons for the SCL-90-R interpersonal sensitivity T-scores were nonsignificant (Table H-3-8(a): p=0.121).

Unadjusted analysis of SCL-90-R interpersonal sensitivity from Models 4 and 5 revealed a significant association between current dioxin and SCL-90-R interpersonal sensitivity T-scores (Table 12-11(g): p=0.022, Est. RR=1.19 and p=0.012, Est. RR=1.18 for Models 4 and 5). Results from the Model 6 unadjusted analysis were marginally significant (p=0.058, Est. RR=1.15). Each analysis showed increases in the percentages of high

Table 12-11.
Analysis of SCL-90-R Interpersonal Sensitivity

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Percent High	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***948***	***10.4***	***1.16 (0.87,1.54)***	***0.343***
	Comparison	***1,279***	***9.2***		
Officer	Ranch Hand	367	4.4	0.91 (0.47,1.73)	0.892
	Comparison	501	4.8		
Enlisted Flyer	Ranch Hand	161	13.7	1.37 (0.73,2.60)	0.417
	Comparison	203	10.3		
Enlisted Groundcrew	Ranch Hand	420	14.5	1.19 (0.82,1.71)	0.411
	Comparison	575	12.5		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	***1.20 (0.90,1.61)***	***0.223***	OCC (p=0.034) DRKYR (p=0.070) EDUC (p=0.128) INC (p<0.001)
Officer	1.00 (0.52,1.92)	0.994	
Enlisted Flyer	1.44 (0.74,2.81)	0.280	
Enlisted Groundcrew	1.21 (0.82,1.76)	0.337	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 12-11. (Continued)
Analysis of SCL-90-R Interpersonal Sensitivity

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	173	11.0	1.09 (0.90,1.33)	0.381
Medium	173	9.8		
High	171	14.0		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
500	1.00 (0.79,1.27)**	0.996**	INIT*OCC (p=0.003) INIT*DRKYR (p=0.028) EDUC (p=0.057) INC (p=0.014) MARITAL (p=0.019) PARENT (p=0.060)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interactions ($p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table H-2-7 for further analysis of these interactions.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 12-11. (Continued)
Analysis of SCL-90-R Interpersonal Sensitivity

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	**n**	**Percent High**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,061	8.7		
Background RH	373	7.5	0.88 (0.57,1.37)	0.575
Low RH	259	9.7	1.11 (0.70,1.77)	0.662
High RH	258	13.6	1.62 (1.06,2.45)	0.024
Low plus High RH	517	11.6	1.36 (0.96,1.92)	0.083

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	**n**	**Adj. Relative Risk (95% C.I.)[ac]**	**p-Value**	**Covariate Remarks**
Comparison	1,031			OCC (p=0.012) DRKYR (p=0.029) INC (p<0.001) MARITAL (p=0.094)
Background RH	359	1.25 (0.79,2.00)	0.342	
Low RH	249	1.11 (0.68,1.84)	0.673	
High RH	251	1.30 (0.84,2.01)	0.234	
Low plus High RH	500	1.22 (0.85,1.75)	0.286	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 12-11. (Continued)
Analysis of SCL-90-R Interpersonal Sensitivity

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent High/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	6.8 (294)	9.7 (299)	13.1 (297)	1.19 (1.03,1.37)	0.022
5	7.0 (299)	9.8 (296)	12.9 (295)	1.18 (1.04,1.35)	0.012
6[c]	7.1 (298)	9.8 (296)	12.9 (295)	1.15 (1.00,1.32)	0.058

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	859	1.05 (0.90,1.22)	0.560	DRKYR (p=0.010) EDUC (p=0.035) INC (p=0.003) MARITAL (p=0.088) PARENT (p=0.038)
5	859	1.06 (0.93,1.21)	0.381	DRKYR (p=0.010) EDUC (p=0.038) INC (p=0.004) MARITAL (p=0.088) PARENT (p=0.040)
6[d]	858	1.02 (0.88,1.18)	0.813	DRKYR (p=0.013) EDUC (p=0.036) INC (p=0.003) MARITAL (p=0.111) PARENT (p=0.031)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

T-scores with increases in current dioxin. Results were nonsignificant for each model after adjustment for lifetime alcohol history, education, current total household income, current marital status, and current parental status (Table 12-11(h): $p>0.38$ for each model).

SCL-90-R Obsessive-Compulsive Behavior

The Model 1 unadjusted group contrast combining all occupations displayed a marginally significant difference in the presence of a high SCL-90-R obsessive-compulsive T-score (Table 12-12(a): $p=0.082$, Est. $RR=1.30$). Of the Ranch Hands, 11.0 percent displayed a high T-score, in contrast to 8.7 percent of the Comparisons. The difference was significant in the adjusted analysis (Table 12-12(b): $p=0.047$, Adj. $RR=1.35$). Significant covariates in the final model were age, occupation, lifetime alcohol history, and current total household income. Contrasts examined within each occupation yielded nonsignificant differences for the unadjusted and adjusted analyses (Table 12-12(a,b): $p>0.14$ for each contrast).

Unadjusted and adjusted analyses of SCL-90-R obsessive-compulsive behavior for Model 2 were nonsignificant (Table 12-12(a,b): $p>0.30$ for both analyses). Current alcohol use, lifetime alcohol history, combat service, and the initial dioxin-by-occupation and initial dioxin-by-current total household income interactions were significant in the final adjusted model. Adjusted results were based on the final model after deletion of the initial dioxin interactions. Results stratified by occupation and current total household income are presented separately in Appendix Table H-2-8.

Significant differences were found between high Ranch Hands and Comparisons in the unadjusted Model 3 analysis of SCL-90-R obsessive-compulsive behavior (Table 12-12(e): $p=0.049$, Est. $RR=1.54$). The adjusted contrast between background Ranch Hands and Comparisons also was significant (Table 12-12(f): $p=0.007$, Adj. $RR=1.79$). Both analyses revealed that a larger percentage of Ranch Hands had high SCL-90-R obsessive-compulsive T-scores than Comparisons (background Ranch Hands: 10.7%; high Ranch Hands: 12.8%; Comparisons: 8.6%). Other Model 3 contrasts were nonsignificant (Table 12-12(e,f): $p>0.17$ for all remaining contrasts). The adjusted analysis displayed the significant covariate effects of occupation, lifetime alcohol history, current total household income, and current employment.

Results from the unadjusted and adjusted analysis of SCL-90-R obsessive-compulsive behavior from Models 4, 5, and 6 indicated that the association between current dioxin and the prevalence of a high T-score was nonsignificant (Table 12-12(g,h): $p>0.29$ for each analysis). Adjusted results for each model are based on the final model after the deletion of the significant interactions of current dioxin-by-current alcohol use and current dioxin-by-current total household income. Other covariates displaying significance in each final model were lifetime alcohol history, education, and current employment. Results stratified by each combination of categories of current alcohol use and current total household income are presented in Appendix Table H-2-8 for each model.

Table 12-12.
Analysis of SCL-90-R Obsessive-Compulsive Behavior

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent High**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***948***	***11.0***	***1.30 (0.98,1.72)***	***0.082***
	Comparison	***1,279***	***8.7***		
Officer	Ranch Hand	367	6.3	1.22 (0.69,2.18)	0.596
	Comparison	501	5.2		
Enlisted Flyer	Ranch Hand	161	14.9	1.37 (0.74,2.53)	0.393
	Comparison	203	11.3		
Enlisted Groundcrew	Ranch Hand	420	13.6	1.30 (0.89,1.91)	0.215
	Comparison	575	10.8		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.35 (1.00,1.80)***	***0.047***	AGE (p=0.023) OCC (p=0.018) DRKYR (p=0.003) INC (p<0.001)
Officer	1.28 (0.71,2.28)	0.412	
Enlisted Flyer	1.45 (0.76,2.74)	0.258	
Enlisted Groundcrew	1.34 (0.90,1.99)	0.149	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 12-12. (Continued)
Analysis of SCL-90-R Obsessive-Compulsive Behavior

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	173	11.6	1.11 (0.91,1.36)	0.304
Medium	173	8.1		
High	171	12.9		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
500	1.05 (0.83,1.34)**	0.674**	INIT*OCC (p=0.017) INIT*INC (p=0.013) ALC (p=0.052) DRKYR (p=0.002) COMBDAYS (p=0.018)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interactions ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table H-2-8 for further analysis of these interactions.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 12-12. (Continued)
Analysis of SCL-90-R Obsessive-Compulsive Behavior

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	**n**	**Percent High**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,061	8.6		
Background RH	373	10.7	1.32 (0.89,1.96)	0.171
Low RH	259	8.9	1.01 (0.62,1.63)	0.982
High RH	258	12.8	1.54 (1.00,2.36)	0.049
Low plus High RH	517	10.8	1.26 (0.89,1.80)	0.196

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	**n**	**Adj. Relative Risk (95% C.I.)[ac]**	**p-Value**	**Covariate Remarks**
Comparison	1,031			OCC (p=0.006) DRKYR (p=0.005) INC (p=0.007) EMPLOY (p=0.030)
Background RH	359	1.79 (1.17,2.73)	0.007	
Low RH	249	0.97 (0.58,1.62)	0.908	
High RH	251	1.26 (0.81,1.97)	0.307	
Low plus High RH	500	1.13 (0.78,1.63)	0.530	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 12-12. (Continued)
Analysis of SCL-90-R Obsessive-Compulsive Behavior

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent High/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	10.2 (294)	10.4 (299)	11.8 (297)	1.02 (0.88,1.18)	0.766
5	10.7 (299)	9.5 (296)	12.2 (295)	1.02 (0.90,1.15)	0.809
6[c]	10.4 (298)	9.5 (296)	12.2 (295)	0.99 (0.87,1.13)	0.893

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	859	0.94 (0.81,1.10)**	0.456**	CURR*ALC (p<0.001) CURR*INC (p=0.013) DRKYR (p=0.005) EDUC (p=0.020) EMPLOY (p=0.077)
5	859	0.95 (0.84,1.08)**	0.461**	CURR*ALC (p<0.001) CURR*INC (p=0.002) DRKYR (p=0.005) EDUC (p=0.022) EMPLOY (p=0.070)
6[d]	858	0.93 (0.81,1.07)**	0.295**	CURR*ALC (p<0.001) CURR*INC (p=0.009) DRKYR (p=0.004) EDUC (p=0.022) EMPLOY (p=0.065)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interactions ($p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table H-2-8 for further analysis of these interactions.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

SCL-90-R Paranoid Ideation

Both Model 1 unadjusted and adjusted analyses displayed a significant group difference in the prevalence of high SCL-90-R paranoid ideation T-scores from the contrast combining all occupations (Table 12-13(a,b): p=0.022, Est. RR=1.55 and p=0.010, Adj. RR=1.65). Marginally significant differences were found in the unadjusted and adjusted enlisted groundcrew contrasts, as well as the adjusted enlisted flyer contrast (Table 12-13(a,b): p=0.073, Est. RR=1.58; p=0.078, Adj. RR=1.55; and p=0.070, Adj. RR=2.23 respectively). Other Model 1 contrasts were nonsignificant (Table 12-13(a,b): p>0.21 for each remaining contrast). Ranch Hands had a greater percentage of high T-scores than Comparisons combining all occupations (Table 12-13(a): 7.0% vs. 4.6%), as well as within each occupation (Table 12-13(a): 3.0% vs. 2.4% for officers, 9.3% vs. 5.4% for enlisted flyers, and 9.5% vs. 6.3% for enlisted groundcrew). Significant covariates present in the final model were occupation, lifetime alcohol history, current total household income, and the group-by-race interaction. Adjusted results are based on the final model after deletion of the interaction, and results stratified by race are presented in Appendix Table H-2-9.

Tests of association between SCL-90-R paranoid ideation and initial dioxin were nonsignificant for both unadjusted and adjusted Model 2 analyses (Table 12-13(c,d): p>0.65 for both analyses). Lifetime alcohol history, education, current total household income, current marital status, current parental status, and combat service were significant covariates in the final adjusted model.

The Model 3 unadjusted analysis revealed significant differences in the prevalence of high SCL-90-R paranoid ideation T-scores when the high Ranch Hands and low plus high Ranch Hands each were contrasted with Comparisons (Table 12-13(e): p=0.010, Est. RR=2.00 and p=0.029, Est. RR=1.64). The percentage of high Ranch Hands, low plus high Ranch Hands, and Comparisons with high T-scores were 8.5, 7.2, and 4.4 percent respectively. The background Ranch Hand contrast was significant and the high Ranch Hand contrast was marginally significant in the adjusted analysis (Table 12-13(f): p=0.007, Adj. RR=2.16 and p=0.090, Adj. RR=1.62). Adjusted results are based on the final model after deletion of the significant interaction between categorized dioxin and current marital status. Other covariates significant in the final model were race, occupation, lifetime alcohol history, and current total household income. After exclusion of occupation from the final model, the high Ranch Hands versus Comparisons contrast was significant, similar to the unadjusted analysis (Appendix Table H-3-7(a): p=0.031, Adj. RR=1.83).

Unadjusted and adjusted analyses of SCL-90-R paranoid ideation for Models 4, 5, and 6 were nonsignificant for tests of association between current dioxin and prevalence of high SCL-90-R paranoid ideation T-scores (Table 12-13(g,h): p≥0.28 for each analysis). Each adjusted model reflected covariate effects of occupation, lifetime alcohol history, current total household income, and current dioxin-by-covariate interactions involving education, current marital status, and combat service. Adjusted results are based on the final models after deletion of the significant current dioxin interactions. Results stratified by education, current marital status, and combat service are presented in Appendix Table H-2-9.

Table 12-13.
Analysis of SCL-90-R Paranoid Ideation

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Percent High	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***948***	***7.0***	***1.55 (1.08,2.22)***	***0.022***
	Comparison	***1,279***	***4.6***		
Officer	Ranch Hand	367	3.0	1.26 (0.55,2.89)	0.740
	Comparison	501	2.4		
Enlisted Flyer	Ranch Hand	161	9.3	1.79 (0.80,4.02)	0.219
	Comparison	203	5.4		
Enlisted Groundcrew	Ranch Hand	420	9.5	1.58 (0.99,2.52)	0.073
	Comparison	575	6.3		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	***1.65 (1.13,2.41)*****	***0.010*****	GROUP*RACE (p=0.044)
Officer	1.46 (0.62,3.42)**	0.386**	OCC (p=0.129)
Enlisted Flyer	2.23 (0.94,5.31)**	0.070**	DRKYR (p<0.001)
Enlisted Groundcrew	1.55 (0.95,2.53)**	0.078**	INC (p<0.001)

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

** Group-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table H-2-9 for further analysis of this interaction.

Table 12-13. (Continued)
Analysis of SCL-90-R Paranoid Ideation

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	173	5.8	1.06 (0.82,1.36)	0.652
Medium	173	8.1		
High	171	7.6		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
500	0.98 (0.74,1.31)	0.914	DRKYR (p=0.002) EDUC (p=0.111) INC (p=0.035) MARITAL (p=0.012) PARENT (p=0.065) COMBDAYS (p=0.017)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 12-13. (Continued)
Analysis of SCL-90-R Paranoid Ideation

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,061	4.4		
Background RH	373	6.2	1.44 (0.86,2.41)	0.170
Low RH	259	5.8	1.31 (0.72,2.38)	0.380
High RH	258	8.5	2.00 (1.18,3.39)	0.010
Low plus High RH	517	7.2	1.64 (1.05,2.57)	0.029

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,031			DXCAT*MARITAL (p=0.032) RACE (p=0.106) OCC (p=0.049) DRKYR (p<0.001) INC (p=0.001)
Background RH	359	2.16 (1.24,3.78)**	0.007**	
Low RH	249	1.29 (0.67,2.47)**	0.451**	
High RH	251	1.62 (0.93,2.82)**	0.090**	
Low plus High RH	500	1.47 (0.92,2.36)**	0.110**	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interaction ($0.01<p\leq0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table H-2-9 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 12-13. (Continued)
Analysis of SCL-90-R Paranoid Ideation

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent High/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	6.1 (294)	5.4 (299)	8.8 (297)	1.08 (0.90,1.28)	0.420
5	6.0 (299)	6.4 (296)	7.8 (295)	1.09 (0.93,1.27)	0.280
6[c]	6.0 (298)	6.4 (296)	7.8 (295)	1.06 (0.90,1.25)	0.506

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	859	0.92 (0.76,1.12)**	0.405**	CURR*EDUC (p=0.027) CURR*MARITAL (p=0.012) CURR*COMBDAYS (p<0.001) OCC (p=0.044) DRKYR (p=0.001) INC (p=0.013)
5	859	0.96 (0.82,1.13)**	0.639**	CURR*EDUC (p=0.017) CURR*MARITAL (p=0.016) CURR*COMBDAYS (p<0.001) OCC (p=0.053) DRKYR (p=0.003) INC (p=0.015)
6[d]	858	0.92 (0.77,1.10)**	0.378**	CURR*EDUC (p=0.023) CURR*MARITAL (p=0.015) CURR*COMBDAYS (p<0.001) OCC (p=0.048) DRKYR (p=0.003) INC (p=0.014)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.
[b] Relative risk for a twofold increase in current dioxin.
[c] Adjusted for log_2 total lipids.
[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interactions ($p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table H-2-9 for further analysis of these interactions.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

SCL-90-R Phobic Anxiety

All contrasts performed from the unadjusted and adjusted analyses of SCL-90-R phobic anxiety displayed nonsignificant results for Model 1 (Table 12-14(a,b): $p>0.53$ for all contrasts). Occupation, lifetime alcohol history, education, current total household income, current employment, and current parental status were significant in the final adjusted model.

The Model 2 unadjusted analysis of SCL-90-R phobic anxiety revealed a significant association between initial dioxin and prevalence of a high SCL-90-R phobic anxiety T-score (Table 12-14(c): $p=0.036$, Est. RR=1.27). Results were marginally significant after covariate adjustment of current alcohol use, lifetime alcohol history, education, current employment, and current marital status (Table 12-14(d): $p=0.051$, Adj. RR=1.27).

The Model 3 unadjusted analysis of SCL-90-R phobic anxiety revealed a marginally significant difference between high Ranch Hands and Comparisons (Table 12-14(e): $p=0.094$, Est. RR=1.47). Adjusted analysis displayed a marginally significant difference between background Ranch Hands and Comparisons (Table 12-14(f): $p=0.094$, Adj. RR=1.52). All remaining Model 3 contrasts were nonsignificant (Table 12-14(e,f): $p>0.41$ for all remaining contrasts). Adjustment for covariates included age, occupation, lifetime alcohol history, education, current total household income, current employment, and current parental status in the final model. When occupation was removed from the final model, the background Ranch Hand versus Comparison contrast became nonsignificant (Appendix Table H-3-11(a): $p=0.229$).

Marginally significant associations between SCL-90-R phobic anxiety and current dioxin were found in the unadjusted analyses of Models 4 and 5 (Table 12-14(g): $p=0.089$, Est. RR=1.15 and $p=0.080$, Est. RR=1.13). The percentage of high SCL-90-R phobic anxiety T-scores increased as current dioxin levels increased. Model 6 unadjusted and adjusted analyses were both nonsignificant, as well as the Model 4 and 5 adjusted analyses (Table 12-14(g,h): $p>0.29$ for each analysis). Occupation, lifetime alcohol history, education, current employment, and current marital status were significant covariates in each adjusted model.

SCL-90-R Psychoticism

All results were nonsignificant for all models analyzed for SCL-90-R psychoticism (Table 12-15(a-h): $p>0.12$ for each analysis). Models 1 and 3 adjusted for age, race, occupation, lifetime alcohol history, and current total household income. Model 3 also adjusted for effects of current employment and the categorized dioxin-by-current alcohol use interaction. Lifetime alcohol history, education, and current marital status were significant covariates in the Model 2 adjusted analysis. Significant in Model 4, 5, and 6 adjusted analyses were occupation, lifetime alcohol history, current total household income, and current employment. Current alcohol use also was significant in Model 5, while the current dioxin-by-current alcohol use interaction was significant in Model 4. Model 3 and 4 results stratified by each category of current alcohol use are presented in Appendix Table H-2-10. Adjusted Model 3 and 4 results are based on the final models after deletion of the significant interaction.

Table 12-14.
Analysis of SCL-90-R Phobic Anxiety

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent High**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***948***	***8.4***	***1.06 (0.78,1.44)***	***0.751***
	Comparison	***1,279***	***8.0***		
Officer	Ranch Hand	367	2.5	0.88 (0.37,2.04)	0.923
	Comparison	501	2.8		
Enlisted Flyer	Ranch Hand	161	10.6	1.21 (0.60,2.44)	0.715
	Comparison	203	8.9		
Enlisted Groundcrew	Ranch Hand	420	12.9	1.06 (0.73,1.56)	0.822
	Comparison	575	12.2		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.10 (0.80,1.52)***	***0.563***	OCC (p<0.001) DRKYR (p=0.148)
Officer	0.99 (0.42,2.36)	0.982	EDUC (p=0.044) INC (p<0.001)
Enlisted Flyer	1.19 (0.58,2.43)	0.642	EMPLOY (p=0.011)
Enlisted Groundcrew	1.10 (0.74,1.63)	0.638	PARENT (p=0.118)

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 12-14. (Continued)
Analysis of SCL-90-R Phobic Anxiety

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	173	5.8	1.27 (1.02,1.58)	0.036
Medium	173	8.7		
High	171	12.3		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
504	1.27 (1.00,1.61)	0.051	ALC (p=0.119) DRKYR (p=0.070) EDUC (p=0.003) EMPLOY (p=0.041) MARITAL (p=0.033)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 12-14. (Continued)
Analysis of SCL-90-R Phobic Anxiety

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,061	7.8		
Background RH	373	7.5	0.98 (0.63,1.54)	0.933
Low RH	259	6.6	0.80 (0.46,1.37)	0.413
High RH	258	11.2	1.47 (0.94,2.31)	0.094
Low plus High RH	517	8.9	1.12 (0.77,1.64)	0.560

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,031			AGE (p=0.078) OCC (p=0.001)
Background RH	359	1.52 (0.93,2.47)	0.094	DRKYR (p=0.095) EDUC (p=0.050)
Low RH	249	0.79 (0.45,1.42)	0.434	INC (p=0.001)
High RH	251	1.02 (0.64,1.64)	0.922	EMPLOY (p=0.008) PARENT (p=0.031)
Low plus High RH	500	0.93 (0.62,1.38)	0.706	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 12-14. (Continued)
Analysis of SCL-90-R Phobic Anxiety

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent High/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	6.5 (294)	7.7 (299)	10.8 (297)	1.15 (0.98,1.35)	0.089
5	6.0 (299)	8.5 (296)	10.5 (295)	1.13 (0.99,1.30)	0.080
6[c]	6.0 (298)	8.5 (296)	10.5 (295)	1.08 (0.93,1.26)	0.293

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	870	0.96 (0.81,1.14)	0.635	OCC (p=0.001) DRKYR (p=0.060) EDUC (p=0.039) EMPLOY (p=0.002) MARITAL (p=0.058)
5	870	0.98 (0.84,1.13)	0.731	OCC (p=0.002) DRKYR (p=0.061) EDUC (p=0.038) EMPLOY (p=0.001) MARITAL (p=0.058)
6[d]	869	0.92 (0.78,1.08)	0.297	OCC (p<0.001) DRKYR (p=0.073) EDUC (p=0.049) EMPLOY (p=0.001) MARITAL (p=0.072)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 12-15.
Analysis of SCL-90-R Psychoticism

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent High**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***948***	***9.6***	***1.10 (0.82,1.46)***	***0.587***
	Comparison	***1,279***	***8.8***		
Officer	Ranch Hand	367	5.2	1.09 (0.59,2.01)	0.920
	Comparison	501	4.8		
Enlisted Flyer	Ranch Hand	161	11.8	1.38 (0.70,2.72)	0.456
	Comparison	203	8.9		
Enlisted Groundcrew	Ranch Hand	420	12.6	1.03 (0.70,1.50)	0.975
	Comparison	575	12.4		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.16 (0.86,1.58)***	***0.329***	AGE (p=0.005) RACE (p=0.133) OCC (p=0.009) DRKYR (p=0.021) INC (p<0.001)
Officer	1.08 (0.57,2.03)	0.815	
Enlisted Flyer	1.57 (0.77,3.19)	0.210	
Enlisted Groundcrew	1.09 (0.73,1.63)	0.674	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 12-15. (Continued)
Analysis of SCL-90-R Psychoticism

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	173	9.8	1.06 (0.86,1.32)	0.587
Medium	173	8.7		
High	171	10.5		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
504	1.07 (0.85,1.35)	0.555	DRKYR (p=0.052) EDUC (p=0.084) MARITAL (p=0.051)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 12-15. (Continued)
Analysis of SCL-90-R Psychoticism

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	**n**	**Percent High**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,061	8.7		
Background RH	373	8.9	1.05 (0.69,1.60)	0.809
Low RH	259	8.5	0.96 (0.59,1.56)	0.852
High RH	258	10.9	1.26 (0.80,1.97)	0.317
Low plus High RH	517	9.7	1.10 (0.77,1.59)	0.598

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	**n**	**Adj. Relative Risk (95% C.I.)[ac]**	**p-Value**	**Covariate Remarks**
Comparison	1,031			DXCAT*ALC (p=0.019) AGE (p=0.050)
Background RH	359	1.43 (0.91,2.25)**	0.122**	RACE (p=0.047) OCC (p=0.005)
Low RH	249	0.90 (0.53,1.54)**	0.704**	DRKYR (p=0.026) INC (p=0.005)
High RH	251	1.12 (0.70,1.80)**	0.636**	EMPLOY (p=0.148)
Low plus High RH	500	1.02 (0.69,1.50)**	0.928**	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table H-2-10 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 12-15. (Continued)
Analysis of SCL-90-R Psychoticism

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent High/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	8.2 (294)	9.4 (299)	10.4 (297)	1.07 (0.92,1.25)	0.371
5	8.7 (299)	8.8 (296)	10.5 (295)	1.08 (0.94,1.23)	0.275
6[c]	8.7 (298)	8.8 (296)	10.5 (295)	1.05 (0.91,1.21)	0.526

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	859	0.95 (0.80,1.13)**	0.559**	CURR*ALC (p=0.036) OCC (p=0.045) DRKYR (p=0.012) INC (p=0.113) EMPLOY (p=0.061)
5	859	0.98 (0.84,1.13)	0.747	OCC (p=0.072) ALC (p=0.150) DRKYR (p=0.027) INC (p=0.103) EMPLOY (p=0.057)
6[d]	858	0.94 (0.81,1.10)	0.471	OCC (p=0.076) DRKYR (p=0.007) INC (p=0.090) EMPLOY (p=0.080)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table H-2-10 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

SCL-90-R Somatization

Significant group differences were found in the Model 1 unadjusted and adjusted analyses of SCL-90-R somatization contrast combining all occupations (Table 12-16(a,b): p=0.048, Est. RR=1.36 and p=0.018, Adj. RR=1.45 for the unadjusted and adjusted analyses). More Ranch Hands (10.2%) than Comparisons (7.7%) had a high SCL-90-R somatization T-score. The adjusted enlisted groundcrew contrast was marginally significant (Table 12-16(b): p=0.081, Adj. RR=1.43). All other contrasts were nonsignificant (Table 12-16(a,b): $p \geq 0.15$ for all remaining contrasts). Covariates in the final adjusted model included occupation, lifetime alcohol history, current total household income, and current employment.

Model 2 analyses of SCL-90-R somatization exhibited a shift from a nonsignificant association with initial dioxin in the unadjusted analysis to a marginally significant association after adjustment for effects of current alcohol use and current marital status (Table 12-16(c,d): p=0.158 and p=0.087, Adj. RR=1.20 respectively).

Unadjusted Model 3 contrasts identified significant differences between high Ranch Hands and Comparisons and between low plus high Ranch Hands and Comparisons (Table 12-16(e): p=0.011, Est. RR=1.75 and p=0.024, Est. RR=1.51 respectively). A greater percentage of Ranch Hands than Comparisons had a high SCL-90-R somatization T-score within each category of Ranch Hands. The background Ranch Hand adjusted contrast revealed that significantly more Ranch Hands than Comparisons exhibited a high SCL-90-R somatization T-score (Table 12-16(f): p=0.031, Adj. RR=1.67). Remaining Model 3 contrasts were nonsignificant (Table 12-16(e,f): $p > 0.10$ for each remaining contrast). Occupation, lifetime alcohol history, current total household income, current employment, and current marital status exhibited significant covariate effects in the final adjusted model. Significance levels of contrasts changed considerably after exclusion of occupation from the final model. The background Ranch Hand contrast became marginally significant (Appendix Table H-3-10(a): p=0.099, Adj. RR=1.47). Nonsignificant results in the original adjusted final model changed to significant results for each of the high and low plus high Ranch Hand contrasts (Appendix Table H-3-13(a): p=0.029, Adj. RR=1.65 and p=0.043, Adj. RR=1.47 respectively). However, education was not included in this auxiliary analysis. When education was added to the final model, the results of the contrasts between high Ranch Hands and Comparisons and between low plus high Ranch Hands and Comparisons for the SCL-90-R somatization T-scores were marginally significant (Appendix Table H-3-14(a): p=0.056, Adj. RR=1.55 and p=0.076, Adj. RR=1.41 respectively).

Unadjusted analysis of SCL-90-R somatization for Models 4 and 5 indicated that high somatization T-scores increased as current dioxin levels increased. Tests of association were marginally significant and significant for Models 4 and 5 respectively (Table 12-16(g): p=0.064, Est. RR=1.15 and p=0.023, Est. RR=1.16 for Models 4 and 5). Results from the adjusted analysis for Models 4 and 5 and both the unadjusted and adjusted analyses for Model 6 were nonsignificant (Table 12-16(g,h): $p > 0.22$ for each analysis). Significant covariates present in each final model include lifetime alcohol history, current total household income, and current marital status, as well as the current dioxin-by-current alcohol use interaction. Education also was significant in Model 5, as was the interaction between

Table 12-16.
Analysis of SCL-90-R Somatization

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent High**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	*Ranch Hand*	*948*	*10.2*	*1.36 (1.01,1.82)*	*0.048*
	Comparison	*1,279*	*7.7*		
Officer	Ranch Hand	367	5.2	1.47 (0.76,2.83)	0.331
	Comparison	501	3.6		
Enlisted Flyer	Ranch Hand	161	12.4	1.30 (0.67,2.51)	0.542
	Comparison	203	9.9		
Enlisted Groundcrew	Ranch Hand	420	13.8	1.35 (0.92,1.98)	0.150
	Comparison	575	10.6		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks**[a]
All	*1.45 (1.07,1.98)*	*0.018*	OCC (p=0.006)
Officer	1.59 (0.80,3.15)	0.183	DRKYR (p=0.079) INC (p<0.001)
Enlisted Flyer	1.39 (0.70,2.76)	0.349	EMPLOY (p=0.025)
Enlisted Groundcrew	1.43 (0.96,2.14)	0.081	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 12-16. (Continued)
Analysis of SCL-90-R Somatization

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	173	8.7	1.16 (0.95,1.41)	0.158
Medium	173	12.1		
High	171	12.9		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
510	1.20 (0.98,1.47)	0.087	ALC (p=0.129) MARITAL (p<0.001)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 12-16. (Continued)
Analysis of SCL-90-R Somatization

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	**n**	**Percent High**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,061	7.6		
Background RH	373	8.6	1.16 (0.75,1.78)	0.505
Low RH	259	9.7	1.27 (0.80,2.04)	0:315
High RH	258	12.8	1.75 (1.14,2.70)	0.011
Low plus High RH	517	11.2	1.51 (1.05,2.15)	0.024

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	**n**	**Adj. Relative Risk (95% C.I.)[ac]**	**p-Value**	**Covariate Remarks**
Comparison	1,031			OCC (p=0.005) DRKYR (p=0.077) INC (p<0.001) EMPLOY (p=0.023) MARITAL (p=0.100)
Background RH	359	1.67 (1.05,2.67)	0.031	
Low RH	249	1.27 (0.76,2.11)	0.369	
High RH	251	1.45 (0.92,2.28)	0.112	
Low plus High RH	500	1.37 (0.94,1.99)	0.107	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 12-16. (Continued)
Analysis of SCL-90-R Somatization

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent High/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	8.2 (294)	9.4 (299)	12.8 (297)	1.15 (0.99,1.33)	0.064
5	7.7 (299)	9.5 (296)	13.2 (295)	1.16 (1.02,1.32)	0.023
6[c]	7.7 (298)	9.5 (296)	13.2 (295)	1.09 (0.95,1.25)	0.227

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	859	1.05 (0.90,1.22)**	0.545**	CURR*ALC (p=0.037) CURR*EDUC (p=0.040) DRKYR (p=0.015) INC (p=0.026) MARITAL (p=0.009)
5	859	1.08 (0.94,1.23)**	0.283**	CURR*ALC (p=0.045) DRKYR (p=0.021) EDUC (p=0.008) INC (p=0.012) MARITAL (p=0.012)
6[d]	858	1.00 (0.87,1.16)**	0.996**	CURR*ALC (p=0.038) CURR*EDUC (p=0.038) DRKYR (p=0.019) INC (p=0.019) MARITAL (p=0.015)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interactions ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table H-2-11 for further analysis of these interactions.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

current dioxin and education in Models 4 and 6. All adjusted results were based on each final model after deletion of the significant current dioxin-by-covariate interactions present in the final models. Results stratified by current alcohol use and education are presented in Appendix Table H-2-11.

SCL-90-R Global Severity Index

Marginally significant differences in the prevalence of high SCL-90-R global severity index T-scores between Ranch Hands and Comparisons in Model 1 were found in the unadjusted overall contrast (Table 12-17(a): p=0.100, Est. RR=1.30). Of the Ranch Hands, 9.8 percent exhibited a high T-score, whereas 7.7 percent of the Comparisons exhibited high T-scores. Adjusted analysis produced significant results for the contrast combining all occupations (Table 12-17(b): p=0.044, Adj. RR=1.38). Differences were nonsignificant when examined within each occupational strata for both the unadjusted and adjusted analyses (Table 12-17(a,b): p>0.12 for each strata). Lifetime alcohol history, education, current total household income, and current marital status were significant covariates in the final adjusted model.

The Model 2 results were nonsignificant for both the unadjusted and adjusted analyses of SCL-90-R global severity index (Table 12-17(c,d): p>0.12 for both analyses). Lifetime alcohol history, education, current marital status, and the initial dioxin-by-current alcohol use interaction were significant in the final model. The adjusted results are based on the final model after deletion of the initial dioxin-by-current alcohol use interaction. Results stratified by each current alcohol use category are presented in Appendix Table H-2-12.

The high and low plus high Ranch Hand categories each demonstrated a greater percentage of high global severity index T-scores than Comparisons in the Model 3 unadjusted analyses (Table 12-17(e): p=0.006, Est. RR=1.82 and p=0.035, Est. RR=1.47 respectively). The high Ranch Hand contrast was marginally significant in the adjusted analysis (Table 12-17(f): p=0.094, Adj. RR=1.47). Results for other Model 3 contrasts were nonsignificant (Table 12-17(e,f): p>0.13 for each remaining contrast). Occupation, lifetime alcohol history, education, current total household income, current employment, and current marital status were significant covariates in the final adjusted model. The high Ranch Hand versus Comparison contrast became significant after occupation was removed from the final model (Appendix Table H-3-15(a): p=0.047, Adj. RR=1.57).

Significant associations between current dioxin and the SCL-90-R global severity index were revealed from the unadjusted analysis of Models 4 and 5 (Table 12-17(g): p=0.024, Est. RR=1.19 and p=0.014, Est. RR=1.18 respectively). Both analyses indicated that the percentage of high global severity index T-scores increased as current dioxin levels increased. Adjusted analyses of Models 4 and 5 were nonsignificant as were both unadjusted and adjusted analyses of Model 6 (Table 12-17(g,h): p>0.11 for all remaining analyses). Models 4, 5, and 6 adjusted for lifetime alcohol use, education, current marital status, and the current dioxin-by-current alcohol use interaction. Current total household income was significant in Model 4 and the interaction between current dioxin and current household income was significant in Models 5 and 6. All adjusted results are based on deletion of the

Table 12-17.
Analysis of SCL-90-R Global Severity Index

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent High**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***948***	***9.8***	***1.30 (0.96,1.74)***	***0.100***
	Comparison	***1,279***	***7.7***		
Officer	Ranch Hand	367	4.6	1.17 (0.60,2.26)	0.771
	Comparison	501	4.0		
Enlisted Flyer	Ranch Hand	161	13.0	1.54 (0.79,3.00)	0.267
	Comparison	203	8.9		
Enlisted Groundcrew	Ranch Hand	420	13.1	1.27 (0.86,1.87)	0.268
	Comparison	575	10.6		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.38 (1.01,1.88)***	***0.044***	DRKYR (p=0.002)
			EDUC (p<0.001)
Officer	1.30 (0.66,2.55)	0.445	INC (p<0.001)
			MARITAL (p=0.020)
Enlisted Flyer	1.73 (0.86,3.48)	0.124	
Enlisted Groundcrew	1.31 (0.87,1.95)	0.195	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 12-17. (Continued)
Analysis of SCL-90-R Global Severity Index

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	173	9.3	1.17 (0.96,1.43)	0.121
Medium	173	10.4		
High	171	14.0		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
504	1.16 (0.94,1.43)**	0.182**	INIT*ALC (p=0.004) DRKYR (p<0.001) EDUC (p=0.038) MARITAL (p=0.002)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interaction ($p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table H-2-12 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 12-17. (Continued)
Analysis of SCL-90-R Global Severity Index

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,061	7.7		
Background RH	373	7.5	1.01 (0.64,1.58)	0.967
Low RH	259	8.9	1.13 (0.70,1.84)	0.615
High RH	258	13.6	1.82 (1.19,2.78)	0.006
Low plus High RH	517	11.2	1.47 (1.03,2.09)	0.035

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,031			OCC (p=0.118) DRKYR (p=0.004) EDUC (p=0.091) INC (p=0.010) EMPLOY (p=0.118) MARITAL (p=0.003)
Background RH	359	1.45 (0.90,2.34)	0.131	
Low RH	249	1.14 (0.68,1.92)	0.615	
High RH	251	1.47 (0.94,2.30)	0.094	
Low plus High RH	500	1.32 (0.91,1.92)	0.148	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 12-17. (Continued)
Analysis of SCL-90-R Global Severity Index

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent High/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	7.5 (294)	8.4 (299)	13.1 (297)	1.19 (1.02,1.38)	0.024
5	7.4 (299)	8.8 (296)	12.9 (295)	1.18 (1.03,1.35)	0.014
6[c]	7.4 (298)	8.8 (296)	12.9 (295)	1.12 (0.97,1.29)	0.118

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	859	1.08 (0.92,1.26)**	0.354**	CURR*ALC (p=0.012) DRKYR (p=0.001) EDUC (p=0.008) INC (p=0.042) MARITAL (p=0.013)
5	859	1.08 (0.95,1.24)**	0.242**	CURR*ALC (p=0.026) CURR*INC (p=0.037) DRKYR (p=0.003) EDUC (p=0.019) MARITAL (p=0.016)
6[d]	858	1.02 (0.88,1.18)**	0.779**	CURR*ALC (p=0.028) CURR*INC (p=0.044) DRKYR (p=0.003) EDUC (p=0.016) MARITAL (p=0.023)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table H-2-12 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

significant interactions from the final models. Appendix Table H-2-12 presents results stratified by current alcohol use and current total household income.

SCL-90-R Positive Symptom Total

Model 1 SCL-90-R positive symptom total results were nonsignificant for both the unadjusted and adjusted analyses (Table 12-18(a,b): $p>0.13$ for all analyses). Occupation, lifetime alcohol history, current total household income, current employment, and current marital status displayed significant covariate effects in the final adjusted model.

Results from both the unadjusted and adjusted analyses of the SCL-90-R positive symptom total were nonsignificant for Model 2 (Table 12-18(c,d): $p>0.17$ for both analyses). Adjusted results are based on the final model after the deletion of the significant initial dioxin-by-occupation and initial dioxin-by-current total household income interactions. Other significant covariates included current alcohol use, lifetime alcohol history, education, current marital status, and current parental status. Results stratified by occupation and current total household income category are presented in Appendix Table H-2-13.

Model 3 unadjusted contrasts revealed a significantly greater prevalence of high SCL-90-R positive symptom total T-scores among high Ranch Hands (14.3%) than Comparisons (9.4%) (Table 12-18(e): $p=0.033$, Est. RR=1.56). This contrast was nonsignificant after adjustment, as were the other Model 3 contrasts both before and after covariate adjustment for occupation, lifetime alcohol history, current total household income, current employment, and current marital status (Table 12-18(e,f): $p>0.11$ for all remaining contrasts). However, exclusion of occupation from the final model revealed a marginally significant difference between high Ranch Hands and Comparisons (Appendix Table H-3-16(b): $p=0.072$, Adj. RR=1.47). However, education was not included in this auxiliary analysis. When education was added to the final model, the results of the contrast between high Ranch Hands and Comparisons for the SCL-90-R positive symptom total T-scores were nonsignificant (Appendix Table H-3-17(a): $p=0.126$).

Significant positive associations between current dioxin and SCL-90-R positive symptom total were found in the unadjusted analysis of Models 4 and 5 (Table 12-18(g): $p=0.027$, Est. RR=1.17 and $p=0.013$, Est. RR=1.17 respectively). Tests of association from the adjusted analyses from Models 4 and 5 and both unadjusted and adjusted analyses of Model 6 were nonsignificant (Table 12-18(g,h): $p>0.14$ for all remaining analyses). Each adjusted model included lifetime alcohol history, education, current total household income, and current marital status. Model 6 additionally adjusted for current alcohol use.

SCL-90-R Positive Symptom Distress Index

All analyses conducted for SCL-90-R positive symptom distress index produced nonsignificant results, except for the Model 5 unadjusted analyses (Table 12-19(a-h): $p>0.11$ for all analyses except Model 5 unadjusted analysis). A marginally significant positive association between current dioxin and a high SCL-90-R positive symptom distress index T-score resulted for the Model 5 unadjusted analysis (Table 12-19(g): $p=0.059$, Est. RR=1.15). Occupation, current total household income, and current parental status were

Table 12-18.
Analysis of SCL-90-R Positive Symptom Total

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	Group	n	Percent High	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***948***	***11.0***	***1.16 (0.88,1.53)***	***0.331***
	Comparison	***1,279***	***9.6***		
Officer	Ranch Hand	367	5.5	0.97 (0.54,1.76)	0.929
	Comparison	501	5.6		
Enlisted Flyer	Ranch Hand	161	13.7	1.37 (0.73,2.60)	0.330
	Comparison	203	10.3		
Enlisted Groundcrew	Ranch Hand	420	14.8	1.17 (0.82,1.69)	0.392
	Comparison	575	12.9		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	***1.25 (0.93,1.66)***	***0.135***	OCC (p=0.009)
Officer	1.06 (0.58,1.93)	0.850	DRKYR (p=0.002) INC (p=0.001)
Enlisted Flyer	1.49 (0.76,2.89)	0.244	EMPLOY (p=0.044)
Enlisted Groundcrew	1.26 (0.86,1.84)	0.241	MARITAL (p=0.029)

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 12-18. (Continued)
Analysis of SCL-90-R Positive Symptom Total

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	173	12.1	1.14 (0.94,1.38)	0.177
Medium	173	9.8		
High	171	15.2		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
	Analysis Results for Log_2 (Initial Dioxin)[c]		
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
500	1.03 (0.82,1.30)**	0.778**	INIT*OCC (p=0.001) INIT*INC (p=0.004) ALC (p=0.059) DRKYR (p=0.003) EDUC (p=0.044) MARITAL (p=0.015) PARENT (p=0.113)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interactions ($p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table H-2-13 for further analysis of these interactions.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 12-18. (Continued)
Analysis of SCL-90-R Positive Symptom Total

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,061	9.4		
Background RH	373	8.6	0.95 (0.62,1.44)	0.791
Low RH	259	10.4	1.08 (0.69,1.70)	0.732
High RH	258	14.3	1.56 (1.04,2.34)	0.033
Low plus High RH	517	12.4	1.31 (0.94,1.84)	0.110

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,031			OCC (p=0.028) DRKYR (p=0.003) INC (p=0.003) EMPLOY (p=0.062) MARITAL (p=0.012)
Background RH	359	1.32 (0.84,2.06)	0.224	
Low RH	249	1.13 (0.70,1.82)	0.614	
High RH	251	1.32 (0.86,2.03)	0.207	
Low plus High RH	500	1.23 (0.87,1.75)	0.247	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 12-18. (Continued)
Analysis of SCL-90-R Positive Symptom Total

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent High/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	8.8 (294)	9.4 (299)	14.1 (297)	1.17 (1.02,1.35)	0.027
5	8.7 (299)	10.1 (296)	13.6 (295)	1.17 (1.03,1.33)	0.013
6[c]	8.7 (298)	10.1 (296)	13.6 (295)	1.10 (0.97,1.27)	0.149

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	859	1.05 (0.91,1.22)	0.494	DRKYR (p=0.011) EDUC (p=0.013) INC (p=0.004) MARITAL (p=0.025)
5	859	1.07 (0.94,1.21)	0.330	DRKYR (p=0.012) EDUC (p=0.014) INC (p=0.004) MARITAL (p=0.025)
6[d]	858	1.00 (0.87,1.15)	0.984	ALC (p=0.130) DRKYR (p=0.006) EDUC (p=0.012) INC (p=0.004) MARITAL (p=0.033)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 12-19.
Analysis of SCL-90-R Positive Symptom Distress Index

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent High**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***948***	***7.8***	***1.04 (0.76,1.43)***	***0.855***
	Comparison	***1,279***	***7.5***		
Officer	Ranch Hand	367	4.6	1.11 (0.58,2.14)	0.884
	Comparison	501	4.2		
Enlisted Flyer	Ranch Hand	161	9.9	0.91 (0.46,1.79)	0.915
	Comparison	203	10.8		
Enlisted Groundcrew	Ranch Hand	420	9.8	1.07 (0.69,1.64)	0.857
	Comparison	575	9.2		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.02 (0.74,1.41)***	***0.881***	OCC (p=0.006) INC (p=0.002) PARENT (p=0.016)
Officer	1.07 (0.55,2.08)	0.847	
Enlisted Flyer	0.90 (0.45,1.80)	0.775	
Enlisted Groundcrew	1.06 (0.69,1.63)	0.797	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 12-19. (Continued)
Analysis of SCL-90-R Positive Symptom Distress Index

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	173	7.5	1.14 (0.91,1.43)	0.248
Medium	173	9.3		
High	171	9.4		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
517	1.18 (0.94,1.48)	0.169	EMPLOY (p=0.115) MARITAL (p=0.062)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 12-19. (Continued)
Analysis of SCL-90-R Positive Symptom Distress Index

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,061	7.2		
Background RH	373	6.2	0.91 (0.56,1.47)	0.691
Low RH	259	7.7	1.06 (0.63,1.77)	0.836
High RH	258	9.7	1.32 (0.82,2.13)	0.249
Low plus High RH	517	8.7	1.19 (0.81,1.75)	0.380

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,046			OCC (p=0.007) INC (p=0.030) PARENT (p=0.004)
Background RH	366	1.07 (0.64,1.78)	0.793	
Low RH	255	1.07 (0.63,1.80)	0.808	
High RH	258	1.04 (0.64,1.70)	0.865	
Low plus High RH	513	1.05 (0.71,1.56)	0.793	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin $\leq$ 10 ppt.
Background (Ranch Hand): Current Dioxin $\leq$ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin $\leq$ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 12-19. (Continued)
Analysis of SCL-90-R Positive Symptom Distress Index

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent High/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	6.1 (294)	7.7 (299)	9.1 (297)	1.14 (0.97,1.35)	0.118
5	5.7 (299)	7.4 (296)	9.8 (295)	1.15 (0.99,1.33)	0.059
6[c]	5.7 (298)	7.4 (296)	9.8 (295)	1.08 (0.92,1.26)	0.359

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	859	1.10 (0.92,1.30)	0.302	DRKYR (p=0.103) INC (p=0.019)
5	859	1.11 (0.95,1.29)	0.172	DRKYR (p=0.105) INC (p=0.022)
6[d]	858	1.03 (0.88,1.22)	0.683	DRKYR (p=0.125) INC (p=0.016)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

significant covariates for Models 1 and 3. Model 2 adjusted for current employment and current marital status. Lifetime alcohol history and current total household income were each included in Models 4, 5, and 6.

DISCUSSION

Prior to the AFHS 1982 Baseline study, little scientifically validated information existed regarding the relationship between dioxin exposure and disturbances of cognition and emotion in man. The Baseline and 1985 followup studies attempted to explore these possible relationships using well-established questionnaires, personality inventories, and neuropsychological assessment techniques. These instruments included the CMI, the MMPI, and the HRB.

Analysis of extensive data generated by the CMI, MMPI and the HRB revealed very few statistically significant differences between those Air Force veterans who sustained dioxin exposure (Ranch Hands) and their unexposed Comparison group. More specifically, the two groups did not differ significantly on tests of cognitive (cerebral) function. The Ranch Hand group reported a moderately greater number of diffuse medical (somatic) complaints on the CMI. They also registered moderately higher (but not statistically significant) scores on those MMPI scales that are influenced most heavily by physical complaints such as generalized feelings of malaise, energy loss, and mental and physical slowing. The herbicide-exposed enlisted groundcrew cohort, which reported the highest levels of exposure, had significantly higher scores than other Ranch Hand group members only on the MMPI depression scale.

Factors contributing to the modest differences between groups were not clearly indicated by estimated dioxin exposure data. It was suspected that observed differences in psychological dependent variables might be related to some combination of negative expectations, anxiety, and increased somatic sensitivity on the part of exposed personnel. As the 1985 followup concluded, the possibility existed that subjectively experienced and reported exposure levels and symptoms were more accurate than exposure data at that time. Subsequently, this exposure data was found to correlate poorly with objectively determined TCDD levels.

A limited number of previous dioxin exposure studies reported findings similar to those described above. Investigations of both military and civilian groups failed to reveal evidence for organic brain dysfunction. However, at least one civilian study reported significantly elevated levels of tension-anxiety and anger-hostility. Psychological tests employed by some of these previous studies were relatively limited. However, the existence of independent data that potentially corroborated the previous AFHS findings indicated the importance of continuing appropriate psychological assessment for the 1987 followup. As the 1985 followup study concluded, participant complaints regarding the lengthy and repetitious psychometric evaluation were noted. Concern regarding potential loss of subjects for the 1987 followup prompted specific changes in the psychometric component of the study. Previously unrevealing and lengthy tests of cognition (i.e., HRB) were suspended. The issue of test-retest boredom was addressed by selecting two new psychometric instruments that

would provide ongoing assessment of important psychological variables while requiring much less time than the MMPI.

The new psychological instruments included the SCL-90-R. This 90-item checklist of physical and mental symptoms provided a reasonable measure of health-related concerns and associated anxiety, depression, and general emotional discomfort. The second test selected was the MCMI. This test provided back-up measures of depression, anxiety, and somatization while also screening for personality disorders and major psychiatric syndromes including psychosis. Both the SCL-90-R and the MCMI were previously employed in clinical and research settings requiring economical assessment of psychiatric disorders, physical disability status, and response to specific therapy. Furthermore, factor analysis and correlational studies indicated that specific scales and factors included in the two new tests correlated reasonably well with comparable elements in the MMPI. Therefore, acceptable continuity of psychological dependent variables was assured.

The addition of data concerning sleep disorders and the 20 scales and 3 indices comprising the SCL-90-R and the MCMI produced a substantial increase in the number of psychological dependent variables requiring analysis for the 1987 followup. Similarly, the number of dependent variable-covariate associations requiring examination increased, as did the probability of a proliferation of statistically significant interactions.

Examination of these psychological dependent variable-covariate associations indicated a host of statistically significant relationships. For example, previously well-known relationships between advancing age and disturbed sleep were noted, as was the well-known phenomena of sleep disturbance following excessive consumption of alcohol. A strong relationship between the presence of PTSD and a disturbance of numerous sleep and psychological variables also was observed. While the number of participants with PTSD was small (approximately 1% of each group), the effects of this condition were striking and made this an important finding. Given logistical difficulties inherent to the study, it was determined that a more efficient assessment of PTSD could be accomplished using a recently developed subscale of the MMPI. While this scale tends to be less precise than the structured psychiatric interview, it was significantly associated with expected psychological endpoints in the covariate adjusted analyses, and it appears to be a useful technique in the assessment of PTSD in population-based studies.

Further inspection of the 1987 data revealed the persistence of several psychological results described as noteworthy in the Baseline and 1985 followup studies. On the SCL-90-R, Ranch Hands demonstrated a statistically greater level of depression than Comparisons and also manifested more physical complaints (somatization) and health-related anxiety. Ranch Hands also recorded higher scores on those MCMI scales thought to reflect antisocial and passive-aggressive traits and psychotic delusional tendencies. However, careful analysis of the MCMI differences determined that these maladaptive traits and symptoms were more probably related to the emergence of psychometric artifacts than the appearance of some new symptoms complex that had not been observed in the previous studies.

The continuing manifestations of depression and health-related complaints and anxiety by members of the Ranch Hand cohort were not surprising. A similar persistence of

entrenched self-reported symptoms had been demonstrated by other populations receiving exposure to known or suspected toxins. Enlisted groundcrew members who reported high levels of herbicide exposure were thought to be particularly vulnerable to repeated public suggestions that negative psychological and physical consequences could be suffered secondary to their exposure. Ranch Hands with psychological make-ups predisposing them to higher levels of anxiety, psychophysiological disturbances and related somatic concerns would predictably demonstrate a self-perpetuating pattern of either static or escalating physical and psychological symptoms. The probability of such a reaction was based in part on previous studies of chronic physical illness. These studies revealed that a significant percentage (5% to 10%) of any medical population is likely to possess a psychological make-up that predisposes them to the development of psychophysiological disturbances and symptom-reactive anxiety that tend to develop in an escalating manner. These same individuals often tend to perceive themselves as unsuccessfully treated and potentially disabled persons. Therefore, they may harbor significant feelings of resentment and hostility that contribute to significantly higher scores on scales reflecting antisocial and passive-aggressive personality traits. On the other hand, moderately elevated scores on such scales and related tendencies toward higher level alcohol consumption could be associated with the presence of "swashbuckling" personality traits that might be perceived as adaptive when viewed in relation to the volunteer and perilous nature of the Ranch Hands' mission in SEA.

As the 1987 examination data was reported in 1990, it was recognized that factors other than dioxin exposure may have contributed to Ranch Hand dependent variable outliers. However, previous studies in clinical medicine suggested that caution was indicated. Studies of medical patients originally diagnosed as suffering from hysteria, hypochondriasis or other "functional disorders" later revealed that these patients were in fact suffering from neurological disease, endocrine dysfunction or other medical disorders approximately 60 percent of the time. Objective monitoring of the study participant's health status over the ensuing years was therefore clearly indicated.

Between 1990 and 1992, objectively determined dioxin body burden levels became available, which allowed extrapolation of initial levels of exposure as well as documentation of current levels. When dependent variables were re-examined in relation to extrapolated initial dioxin levels, a number of statistically significant results emerged for the verified questionnaire, sleep disorder, and SCL-90-R variables. However, when adjusted for effective covariate factors (i.e., age, education, alcohol use, and race), none of these results remained significant. On the other hand, 9 of the 20 MCMI scales remained statistically significant. Careful analyses of the MCMI findings revealed the absence of predicted correlation between the MCMI results and other dependent variable data including verified questionnaire and SCL-90-R results. Furthermore, exploration of MCMI test construction intricacies also suggested the probability of a spurious statistical relationship between MCMI scale results and initial dioxin analyses.

Examination of current dioxin and time since tour analyses for the verified questionnaire and sleep disorder variables generally were found to be nonsignificant. Comparable analysis of the SCL-90-R variables revealed two statistically significant results including a positive relationship between anxiety scale elevation and current dioxin levels for Ranch Hands with

greater than 18.6 years of service. However, additional inspection of verified questionnaire data failed to reveal corroborating evidence.

When adjusted analyses of the MCMI variables were examined in relation to the high current dioxin category, only two statistically significant results emerged (i.e., schizoid and schizo-typal scales). Previously discussed factors relating to test structure and absence of any corroborating verified questionnaire data combined to reduce the likelihood that these results were associated with a dose-response effect. By the time the objectively determined dioxin analyses could be completed, the 1992 followup study psychological instruments were essentially in place. Dependent variable measures remained unchanged and included the five verified questionnaire categories, the sleep disorder questionnaire, the SCL-90-R, the MCMI. As reported above, covariate factors were expanded by the inclusion of five new factors including combat service. Statistical models also were modified as indicated above in order to allow a more sophisticated within group analysis of both initial and current TCDD levels in the Ranch Hand group.

As analysis of the 1992 followup data proceeded, the addition of new covariates resulted in an expanded number of previously unexplored and potentially significant relationships. The SCL-90-R was retained for statistical analysis because of its effectiveness as a co-measure of variables included in the verified questionnaire. Given its historical relationship to the MCMI, the SCL-90-R also was retained to maintain psychometric continuity across the four phases of the AFHS completed to date.

As revealed in the summary tables of the 1992 followup study, the Model 1 analysis contrasted Ranch Hands and Comparisons across all occupations and within each occupation. With the exception of the other neuroses variable, all significant differences were found by combining and contrasting all Ranch Hand and Comparison occupations in both the unadjusted and adjusted analyses. On the unadjusted analysis statistically significant results were observed on the SCL-90-R hostility, paranoid ideation, and somatization scales with tendencies toward significance demonstrated on the anxiety, obsessive-compulsive behavior, and global severity index scales. Adjusted Model 1 data revealed marginally significant elevations for enlisted groundcrew or enlisted flyers on the anxiety, hostility, paranoid ideation, and somatization SCL-90-R scales as well as a continued significant elevation on the other neuroses variable. When all occupation categories were combined, the number of statistically significant scale elevations increased. Significant results were obtained on the other neuroses indicator as well as the anxiety, obsessive-compulsive behavior, paranoid ideation, somatization, and global severity index subscales of the SCL-90-R.

The persistence of elevated indicators of psychological distress for the adjusted Model 1 data is probably best understood when viewed in relation to dependent variable data obtained from Models 3, 4, 5, and 6. Like Model 1, Model 3 contrasted Ranch Hand versus Comparison dependent variable data calculated in relation to categorized dioxin levels. Ranch Hands demonstrating high levels of dioxin obtained SCL-90-R scaled scores that were statistically higher than those obtained by Comparisons on a consistent basis. Essentially, all but two of the SCL-90-R scales reached the level of statistical significance (see Table 12-22). In addition, significant scores were obtained on the anxiety and other neuroses scales obtained from the verified questionnaire data. Adjusted analyses revealed a dramatic change

as only the anxiety scale of the SCL-90-R remained statistically significant and three additional scales remained marginally significant.

The above results highlight the important impact of covariate factors such as occupation and lifetime alcohol history upon dependent variable outcomes. For example, examination of SCL-90-R anxiety scale results across models reveals statistically significant unadjusted and/or adjusted scale elevations on essentially all models. Inspection of dependent variable-covariate associations for psychological assessment appearing in Appendix Table H-1-1 demonstrate the extent to which these anxiety scale elevations were influenced by occupational status. An average of 9.1 percent of enlisted groundcrew and enlisted flyers obtained significant scores on this scale, while only 2.9 percent of the officers obtained comparable results. This is not to say that all dependent variable-covariate associations were significant. For example, combat service was not significantly associated with any dependent variable outcome.

The current dioxin level analyses for Ranch Hands offer a unique opportunity to clearly assess dose-response relationships essentially in the absence of potentially confounding covariate factors. The unadjusted psychological data for Models 4, 5, and 6 again revealed statistically significant outcomes on six of the SCL-90-R scales and the other neuroses and anxiety verified questionnaire scales. These results are highly similar to those obtained on the Model 3 analysis where symptoms of anxiety, tension, hostility, somatization and generalized psychological distress were endorsed with significant frequency. Marginally significant elevations also were found on the somatization, phobic anxiety, and positive symptom distress index of Models 4 and 5. The Model 6 analyses found generally fewer significant results. Adjusted analyses of Models 4, 5, and 6 were nonsignificant with one minor exception. The essential absence of statistically significant adjusted test results observed in Models 4, 5, and 6 suggest that the statistically significant adjusted test results observed in Models 1 and 3 can be explained on the basis of factors other than a causal relationship with TCDD body burdens. Notably, the residual presence of statistically significant Ranch Hand psychological test scores is reminiscent of the results obtained on the 1982 and followup 1985 and 1987 studies.

As reported in the previous studies, a significant portion of the enlisted men continued to endorse test items reflecting higher levels of anxiety and somatic complaints with persistent health-related apprehension. Concern about their current symptoms and future life has probably been heightened by self-estimated or substantiated exposure to dioxin. Some of these Ranch Hands have evidently developed both conscious or unconscious forms of anticipatory anxiety with a related tendency to associate almost any psychological or physical symptom they might experience with their self-perceived dioxin exposure. While some of their fears regarding negative future outcomes may have abated over the years, residual apprehension, and perhaps resentment and hostility, remain. Conscious and unconscious feelings of this type tend to be maximal while undergoing followup medical and psychological evaluation. Anxiety and related psychophysiological disturbances probably also have been heightened by sometimes negative and sensationalized media reports concerning possible outcomes associated with dioxin exposure. As noted in the introduction of this chapter, a previously completed Veteran's Administration study (22) found that those veterans reporting "high level" exposure to Agent Orange are most likely to demonstrate

poor morale, anxiety, organic symptoms, hostility or fear of possible injury or losing control. Notably, those veterans reporting high levels of exposure and related levels of psychological distress failed to differ from low exposure veterans on objective measures of psychological status or cognitive function. Similarly, those Ranch Hands who obtained statistically significant symptom scale elevations on the adjusted results, failed to demonstrate clear-cut evidence of verified psychological disorders.

In conclusion, these data further suggest that factors other than dioxin exposure continue to contribute to a relatively small but notable number of Ranch Hand test score abnormalities. However, previous studies in clinical medicine continue to indicate the need for caution when interpreting the outcome of large group statistical studies. While such undertakings increase the probability of obtaining reliable and valid results, the possibility that a small subset of physically or psychologically vulnerable Ranch Hands may have suffered psychological injury in the context of their exposure to dioxin cannot be unequivocally ruled out at this time.

SUMMARY

Verified psychological conditions and the SCL-90-R inventory of nine primary symptom dimensions and three global indices of distress were examined in the psychological assessment. Each endpoint was tested for any relationship with group (Model 1), initial dioxin (Model 2), categorized dioxin (Model 3), current lipid-adjusted dioxin (Model 4), current whole-weight dioxin (Model 5), and current whole-weight dioxin adjusted for total lipids (Model 6). Results are summarized and presented in Tables 12-20 through 12-23. A summary of group-by-covariate and dioxin-by-covariate interactions is found in Table 12-24.

Model 1: Group Analysis

The Model 1 analysis contrasted Ranch Hands and Comparisons across all occupations and within each occupation. With the exception of the other neuroses variable, all significant differences found were from the contrasts combining all occupations in both the unadjusted and adjusted analyses. The other neuroses variable displayed significant differences for both enlisted groundcrew contrasts as well as the adjusted contrast for all participants. Also, all significant results revealed more Ranch Hands than Comparisons either had a higher percentage of histories of other neuroses or a greater prevalence of high SCL-90-R T-scores. Variables revealing significant or marginally significant differences were other neuroses, SCL-90-R anxiety, SCL-90-R hostility, SCL-90-R obsessive-compulsive behavior, SCL-90-R paranoid ideation, SCL-90-R somatization, and SCL-90-R global severity index. Unadjusted significant or marginally significant results were either from the contrasts combining all occupations or the enlisted groundcrew contrasts. The enlisted flyer contrasts of the adjusted analysis also revealed marginally significant differences.

Model 2: Initial Dioxin Analysis

Significant results in the unadjusted tests of association between the psychological endpoints and initial dioxin tests occurred only for the SCL-90-R phobic anxiety symptom dimension. The results indicate a positive association between initial dioxin and high SCL-90-R phobic anxiety T-scores. The adjusted analysis of SCL-90-R phobic anxiety was

Table 12-20.
Summary of Group Analyses (Model 1) for Psychology Variables
(Ranch Hands vs. Comparisons)

Variable	UNADJUSTED All	Officer	Enlisted Flyer	Enlisted Groundcrew
Verified Medical Records				
Psychoses	ns	ns	NS	ns
Alcohol Dependence	NS	ns	NS	NS
Drug Dependence	ns	--	--	ns
Anxiety	NS	NS	NS	NS
Other Neuroses	NS	ns	NS	+0.040
Psychological Examination				
SCL-90-R Anxiety	NS*	NS	NS	NS
SCL-90-R Depression	NS	NS	NS	NS
SCL-90-R Hostility	+0.044	ns	NS	NS*
SCL-90-R Interpersonal Sensitivity	NS	ns	NS	NS
SCL-90-R Obsessive-Compulsive Behavior	NS*	NS	NS	NS
SCL-90-R Paranoid Ideation	+0.022	NS	NS	NS*
SCL-90-R Phobic Anxiety	NS	ns	NS	NS
SCL-90-R Psychoticism	NS	NS	NS	NS
SCL-90-R Somatization	+0.048	NS	NS	NS
SCL-90-R Global Severity Index	NS*	NS	NS	NS
SCL-90-R Positive Symptom Total	NS	ns	NS	NS
SCL-90-R Positive Symptom Distress Index	NS	NS	ns	NS

+: Relative risk ≥ 1.00.
--: Analysis not performed due to sparse number of abnormalities.
NS or ns: Not significant ($p>0.10$).
NS*: Marginally significant ($0.05<p\leq0.10$).
Note: P-value given if $p\leq0.05$.
A capital "NS" denotes a relative risk 1.00 or greater; a lower case "ns" denotes relative risk less than 1.00.

Table 12-20. (Continued)
Summary of Group Analyses (Model 1) for Psychology Variables
(Ranch Hands vs. Comparisons)

Variable	ADJUSTED			
	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Verified Medical Records				
Psychoses	NS	NS	NS	ns
Alcohol Dependence	**(NS)	**(ns)	**(NS)	**(NS)
Drug Dependence	ns	--	--	ns
Anxiety	NS	NS	NS	NS
Other Neuroses	**(+0.034)	**(NS)	**(NS)	**(+0.017)
Psychological Examination				
SCL-90-R Anxiety	+0.039	NS	NS*	NS
SCL-90-R Depression	NS	NS	NS	NS
SCL-90-R Hostility	**(NS*)	**(ns)	**(NS*)	**(NS)
SCL-90-R Interpersonal Sensitivity	NS	NS	NS	NS
SCL-90-R Obsessive-Compulsive Behavior	+0.047	NS	NS	NS
SCL-90-R Paranoid Ideation	**(+0.010)	**(NS)	**(NS*)	**(NS*)
SCL-90-R Phobic Anxiety	NS	ns	NS	NS
SCL-90-R Psychoticism	NS	NS	NS	NS
SCL-90-R Somatization	+0.018	NS	NS	NS*
SCL-90-R Global Severity Index	+0.044	NS	NS	NS
SCL-90-R Positive Symptom Total	NS	NS	NS	NS
SCL-90-R Positive Symptom Distress Index	NS	NS	ns	NS

+: Relative risk $\geq$ 1.00.
--: Analysis not performed due to sparse number of abnormalities.
NS or ns: Not significant ($p>0.10$).
NS*: Marginally significant ($0.05<p\leq0.10$).
**(NS) or **(ns): Group-by-covariate interaction ($p\leq0.05$); not significant when interaction is deleted; refer to Appendix H-2 for further analysis of this interaction.
**(NS*): Group-by-covariate interaction ($p\leq0.05$); marginally significant when interaction is deleted; refer to Appendix H-2 for further analysis of this interaction.
**(...): Group-by-covariate interaction ($p\leq0.05$); significant when interaction is deleted and p-value is given in parentheses; refer to Appendix H-2 for further analysis of this interaction.

Note: A capital "NS" denotes a relative risk 1.00 or greater; a lower case "ns" denotes relative risk less than 1.00.

Table 12-21.
Summary of Initial Dioxin Analyses (Model 2) for Psychology Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
Verified Medical Records		
Psychoses	ns	ns
Alcohol Dependence	NS	NS
Drug Dependence	--	--
Anxiety	NS	**(ns)
Other Neuroses	NS	NS
Psychological Examination		
SCL-90-R Anxiety	NS	**(NS)
SCL-90-R Depression	NS	**(NS)
SCL-90-R Hostility	NS*	NS
SCL-90-R Interpersonal Sensitivity	NS	**(NS)
SCL-90-R Obsessive-Compulsive Behavior	NS	**(NS)
SCL-90-R Paranoid Ideation	NS	ns
SCL-90-R Phobic Anxiety	+0.036	NS*
SCL-90-R Psychoticism	NS	NS
SCL-90-R Somatization	NS	NS*
SCL-90-R Global Severity Index	NS	**(NS)
SCL-90-R Positive Symptom Total	NS	**(NS)
SCL-90-R Positive Symptom Distress Index	NS	NS

+: Relative risk $\geq$ 1.00.
--: Analysis not performed due to sparse number of abnormalities.
NS or ns: Not significant ($p>0.10$).
NS*: Marginally significant ($0.05<p\leq0.10$).
**(NS) or **(ns): Log_2 (initial dioxin)-by-covariate interaction ($p\leq0.05$); not significant when interaction is deleted; refer to Appendix H-2 for further analysis of this interaction.
Note: P-value given if $p\leq0.05$.
A capital "NS" denotes a relative risk of 1.00 or greater; lower case "ns" denotes relative risk less than 1.00.

Table 12-22.
Summary of Categorized Dioxin Analyses (Model 3) for Psychology Variables (Ranch Hands vs. Comparisons)

	UNADJUSTED			
Variable	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Verified Medical Records				
Psychoses	ns	NS	NS	NS
Alcohol Dependence	NS	NS	NS	NS
Drug Dependence	ns	--	--	--
Anxiety	ns	ns	+0.044	NS
Other Neuroses	ns	NS*	+0.037	+0.010
Psychological Examination				
SCL-90-R Anxiety	ns	NS	+0.002	+0.009
SCL-90-R Depression	NS	ns	+0.031	NS
SCL-90-R Hostility	NS	NS	+0.008	+0.032
SCL-90-R Interpersonal Sensitivity	ns	NS	+0.024	NS*
SCL-90-R Obsessive-Compulsive Behavior	NS	NS	+0.049	NS
SCL-90-R Paranoid Ideation	NS	NS	+0.010	+0.029
SCL-90-R Phobic Anxiety	ns	ns	NS*	NS
SCL-90-R Psychoticism	NS	ns	NS	NS
SCL-90-R Somatization	NS	NS	+0.011	+0.024
SCL-90-R Global Severity Index	NS	NS	+0.006	+0.035
SCL-90-R Positive Symptom Total	ns	NS	+0.033	NS
SCL-90-R Positive Symptom Distress Index	ns	NS	NS	NS

+: Relative risk ≥ 1.00.
--: Analysis not performed due to sparse number of abnormalities.
NS or ns: Not significant ($p>0.10$).
NS*: Marginally significant ($0.05<p\leq0.10$).
Note: P-value given if $p\leq0.05$.
A capital "NS" denotes a relative risk 1.00 or greater; a lower case "ns" denotes relative risk less than 1.00.

Table 12-22. (Continued)
Summary of Categorized Dioxin Analyses (Model 3) for Psychology Variables (Ranch Hands vs. Comparisons)

	ADJUSTED			
Variable	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Verified Medical Records				
Psychoses	ns	NS	ns	NS
Alcohol Dependence	NS	NS	NS	NS
Drug Dependence	NS	--	--	--
Anxiety	NS	ns	NS	ns
Other Neuroses	**(NS)	**(NS)	**(NS)	**(NS)
Psychological Examination				
SCL-90-R Anxiety	NS	NS	+0.041	NS*
SCL-90-R Depression	NS	ns	NS	NS
SCL-90-R Hostility	NS	NS	NS*	NS
SCL-90-R Interpersonal Sensitivity	NS	NS	NS	NS
SCL-90-R Obsessive-Compulsive Behavior	+0.007	ns	NS	NS
SCL-90-R Paranoid Ideation	**(+0.007)	**(NS)	**(NS*)	**(NS)
SCL-90-R Phobic Anxiety	NS*	ns	NS	ns
SCL-90-R Psychoticism	**(NS)	**(ns)	**(NS)	**(NS)
SCL-90-R Somatization	+0.031	NS	NS	NS
SCL-90-R Global Severity Index	NS	NS	NS*	NS
SCL-90-R Positive Symptom Total	NS	NS	NS	NS
SCL-90-R Positive Symptom Distress Index	NS	NS	NS	NS

+: Relative risk ≥ 1.00.
--: Analysis not performed due to sparse number of abnormalities.
NS or ns: Not significant ($p > 0.10$).
NS*: Marginally significant ($0.05 < p \leq 0.10$).
**(NS) or **(ns): Categorized dioxin-by-covariate interaction ($p \leq 0.05$); not significant when interaction is deleted; refer to Appendix H-2 for further analysis of this interaction.
**(NS*): Categorized dioxin-by-covariate interaction ($p \leq 0.05$); marginally significant when interaction is deleted; refer to Appendix H-2 for further analysis of this interaction.
**(+0.007): Categorized dioxin-by-covariate interaction ($p \leq 0.05$); significant ($p = 0.007$) when interaction is deleted; refer to Appendix H-2 for further analysis of this interaction.
Note: P-value given if $p \leq 0.05$.
A capital "NS" denotes a relative risk 1.00 or greater; a lower case "ns" denotes relative risk less than 1.00.

Table 12-23.
Summary of Current Dioxin Analyses (Models 4, 5, and 6) for Psychology Variables (Ranch Hands Only)

Variable	UNADJUSTED		
	Model 4: Lipid-Adjusted Current Dioxin	Model 5: Whole-Weight Current Dioxin	Model 6: Whole-Weight Current Dioxin Adjusted for Total Lipids
Verified Medical Records			
Psychoses	NS	NS	NS
Alcohol Dependence	ns	ns	ns
Drug Dependence	ns	ns	ns
Anxiety	NS*	+0.041	NS
Other Neuroses	+0.013	+0.005	NS
Psychological Examination			
SCL-90-R Anxiety	+0.005	+0.002	+0.013
SCL-90-R Depression	NS	NS	NS
SCL-90-R Hostility	+0.008	+0.004	+0.019
SCL-90-R Interpersonal Sensitivity	+0.022	+0.012	NS*
SCL-90-R Obsessive-Compulsive Behavior	NS	NS	ns
SCL-90-R Paranoid Ideation	NS	NS	NS
SCL-90-R Phobic Anxiety	NS*	NS*	NS
SCL-90-R Psychoticism	NS	NS	NS
SCL-90-R Somatization	NS*	+0.023	NS
SCL-90-R Global Severity Index	+0.024	+0.014	NS
SCL-90-R Positive Symptom Total	+0.027	+0.013	NS
SCL-90-R Positive Symptom Distress Index	NS	NS*	NS

+: Relative risk $\geq$ 1.00.
NS or ns: Not significant ($p>0.10$).
NS*: Marginally significant ($0.05<p\leq0.10$).
Note: P-value given if $p\leq0.05$.
A capital "NS" denotes a relative risk of 1.00 or greater; a lower case "ns" denotes relative risk less than 1.00.

Table 12-23. (Continued)
Summary of Current Dioxin Analyses (Models 4, 5, and 6) for Psychology Variables (Ranch Hands Only)

	ADJUSTED		
Variable	Model 4: Lipid-Adjusted Current Dioxin	Model 5: Whole-Weight Current Dioxin	Model 6: Whole-Weight Current Dioxin Adjusted for Total Lipids
Verified Medical Records			
Psychoses	NS	NS	ns
Alcohol Dependence	ns*	ns	-0.036
Drug Dependence	--	--	--
Anxiety	ns	ns	ns
Other Neuroses	**(ns)	**(NS)	**(ns)
Psychological Examination			
SCL-90-R Anxiety	**(NS)	**(NS*)	**(NS)
SCL-90-R Depression	**(NS)	**(NS)	**(ns)
SCL-90-R Hostility	NS	NS	NS
SCL-90-R Interpersonal Sensitivity	NS	NS	NS
SCL-90-R Obsessive-Compulsive Behavior	**(ns)	**(ns)	**(ns)
SCL-90-R Paranoid Ideation	**(ns)	**(ns)	**(ns)
SCL-90-R Phobic Anxiety	ns	ns	ns
SCL-90-R Psychoticism	**(ns)	ns	ns
SCL-90-R Somatization	**(NS)	**(NS)	**(NS)
SCL-90-R Global Severity Index	**(NS)	**(NS)	**(NS)
SCL-90-R Positive Symptom Total	NS	NS	NS
SCL-90-R Positive Symptom Distress Index	NS	NS	NS

-: Relative risk < 1.00.
--: Analysis not performed due to sparse number of abnormalities.
NS or ns: Not significant ($p>0.10$).
ns*: Marginally significant ($0.05<p\leq 0.10$).
**(NS) or **(ns): Log_2 (current dioxin + 1)-by-covariate interaction ($p\leq 0.05$); not significant when interaction is deleted; refer to Appendix H-2 for further analysis of this interaction.
**(NS*): Log_2 (current dioxin + 1)-by-covariate interaction ($p\leq 0.05$); marginally significant when interaction is deleted; refer to Appendix H-2 for further analysis of this interaction.
Note: P-value given if $p\leq 0.05$.
A capital "NS" denotes a relative risk of 1.00 or greater; a lower case "ns" denotes relative risk less than 1.00.

Table 12-24.
Summary of Group-by-Covariate and Dioxin-by-Covariate Interactions from Adjusted Analyses of Psychology Variables

Model	Variable	Covariate
1[a]	Alcohol Dependence	Current Marital Status
	Other Neuroses	Education, Current Total Household Income
	SCL-90-R Hostility	Current Alcohol Use, Education
	SCL-90-R Paranoid Ideation	Race
2[b]	Anxiety	Occupation
	SCL-90-R Anxiety	Occupation, Current Alcohol Use
	SCL-90-R Depression	Lifetime Alcohol History
	SCL-90-R Interpersonal Sensitivity	Occupation, Lifetime Alcohol History
	SCL-90-R Obsessive-Compulsive Behavior	Occupation, Current Total Household Income
	SCL-90-R Global Severity Index	Current Alcohol Use
	SCL-90-R Positive Symptom Total	Occupation, Current Total Household Income
3[c]	Other Neuroses	Lifetime Alcohol History, Education, Current Total Household Income, Combat Service
	SCL-90-R Paranoid Ideation	Current Marital Status
	SCL-90-R Psychoticism	Current Alcohol Use
4[d]	Other Neuroses	Lifetime Alcohol History
	SCL-90-R Anxiety	Current Alcohol Use
	SCL-90-R Depression	Current Total Household Income
	SCL-90-R Obsessive-Compulsive Behavior	Current Alcohol Use, Current Total Household Income
	SCL-90-R Paranoid Ideation	Education, Current Marital Status, Combat Service
	SCL-90-R Psychoticism	Current Alcohol Use
	SCL-90-R Somatization	Current Alcohol Use, Education
	SCL-90-R Global Severity Index	Current Alcohol Use
5[e]	Other Neuroses	Lifetime Alcohol History
	SCL-90-R Anxiety	Current Alcohol Use
	SCL-90-R Depression	Race, Current Total Household Income
	SCL-90-R Obsessive-Compulsive Behavior	Current Alcohol Use, Current Total Household Income
	SCL-90-R Paranoid Ideation	Education, Current Marital Status, Combat Service
	SCL-90-R Somatization	Current Alcohol Use
	SCL-90-R Global Severity Index	Current Alcohol Use, Current Total Household Income

Table 12-24. (Continued)
Summary of Group-by-Covariate and Dioxin-by-Covariate Interactions from Adjusted Analyses of Psychology Variables

Model	Variable	Covariate
6[f]	Other Neuroses	Lifetime Alcohol History
	SCL-90-R Anxiety	Current Alcohol Use
	SCL-90-R Depression	Race, Current Total Household Income
	SCL-90-R Obsessive-Compulsive Behavior	Current Alcohol Use, Current Total Household Income
	SCL-90-R Paranoid Ideation	Education, Current Marital Status, Combat Service
	SCL-90-R Somatization	Current Alcohol Use, Education
	SCL-90-R Global Severity Index	Current Alcohol Use, Current Total Household Income

[a] Group Analysis (Ranch Hands vs. Comparison).
[b] Ranch Hands—Log_2 (Initial Dioxin).
[c] Categorized Dioxin.
[d] Ranch Hands—Log_2 (Current Lipid-Adjusted Dioxin + 1).
[e] Ranch Hands—Log_2 (Current Whole-Weight Dioxin + 1).
[f] Ranch Hands—Log_2 (Current Whole-Weight Dioxin + 1), Adjusted for Total Lipids.

marginally significant. Other marginally significant analyses were SCL-90-R hostility (unadjusted) and SCL-90-R somatization (adjusted).

Model 3: Categorized Dioxin Analysis

Unadjusted Model 3 analyses revealed many significant differences between high Ranch Hands and Comparisons and between low plus high Ranch Hands and Comparisons. Other neuroses, SCL-90-R anxiety, SCL-90-R hostility, SCL-90-R paranoid ideation, SCL-90-R somatization, and SCL-90-R global severity index were each significant for both contrasts. Anxiety, SCL-90-R depression, SCL-90-R interpersonal sensitivity, SCL-90-R obsessive-compulsive behavior, and SCL-90-R positive symptom total each demonstrated significant differences for the high Ranch Hand contrast only. Marginally significant results were found from the low Ranch Hand contrast examining other neuroses, the high Ranch Hand contrast examining SCL-90-R phobic anxiety, and the low plus high contrast examining SCL-90-R interpersonal sensitivity. Each significant and marginally significant resulting contrast revealed Ranch Hands exhibited the greater history of verified psychological conditions or a greater percentage of high T-scores for the SCL-90-R inventory variables.

Adjusted analyses of Model 3 varied greatly from the unadjusted analyses. Most of the significant results were from the background Ranch Hands contrasts and resulted from the analyses of SCL-90-R obsessive-compulsive behavior, SCL-90-R paranoid ideation, and SCL-90-R somatization. The SCL-90-R phobic anxiety result was marginally significant for the background Ranch Hand contrast. Differences between high Ranch Hands and Comparisons were significant only for the SCL-90-R anxiety analysis. Marginally significant differences were revealed from the high Ranch Hands versus Comparisons contrast for SCL-90-R hostility, SCL-90-R paranoid ideation, and SCL-90-R global severity index. Marginally significant differences were uncovered from the low plus high Ranch Hand versus Comparison contrast for SCL-90-R anxiety. Similar to the unadjusted analyses, all significant and marginally significant contrasts revealed that Ranch Hands had the larger percentage of high SCL-90-R T-scores.

Models 4, 5, and 6: Current Dioxin Analyses

Unadjusted analysis results of Models 4 and 5 closely resembled each other, but Model 6 analyses found fewer significant results. Models 4 and 5 each displayed significant current dioxin associations with other neuroses, SCL-90-R anxiety, SCL-90-R hostility, SCL-90-R interpersonal sensitivity, SCL-90-R global severity index, and SCL-90-R positive symptom total in the unadjusted analyses. Unadjusted analyses of anxiety and SCL-90-R somatization displayed marginally significant results in Model 4 and significant results in Model 5. SCL-90-R phobic anxiety was marginally significant in Models 4 and 5. The SCL-90-R positive symptom distress index was marginally significant for Model 5 only. Only SCL-90-R anxiety and SCL-90-R hostility showed significant current dioxin associations from Model 6 unadjusted analyses, and SCL-90-R interpersonal sensitivity displayed a marginally significant association with current dioxin from Model 6. All significant and marginally significant results revealed that the history of a verified psychological condition or the prevalence of high T-scores for the SCL-90-R inventory variables increased as current dioxin levels increased.

In contrast to the unadjusted analyses of Models 4, 5, and 6, most associations from the adjusted analyses were nonsignificant. Only one current dioxin association, which was from the Model 6 analysis of alcohol dependence, was significant. Model 4 results were marginally significant for alcohol dependence only. Both analyses revealed an inverse association where the history of alcohol dependence decreased as the current dioxin level increased. A marginally significant positive association also was found from the Model 5 adjusted analysis of SCL-90-R anxiety.

CONCLUSION

Most Model 1 significant results were from contrasts combining all occupations and among the SCL-90-R inventory variables. All significant differences from Model 1 contrasts found that Ranch Hands exhibited higher psychological distress than Comparisons.

No significant differences were observed based on the Model 2 initial dioxin adjusted analyses, and only two of the SCL-90-R measures were marginally significant. Significant results from Model 3 unadjusted analysis were found exclusively within the high or low plus high Ranch Hand versus Comparisons contrasts. Adjusted Model 3 analysis revealed only three significant SCL-90-R endpoints and were found within the background Ranch Hand versus Comparisons contrasts. All significant differences from Model 3 contrasts found that Ranch Hands exhibited higher psychological distress than Comparisons.

Notable among analyses of Models 4, 5, and 6 were the similarities among Models 4 and 5 and their differences with Model 6 results. Unadjusted analysis of Models 4 and 5 displayed several positive significant associations between psychological distress and current dioxin levels while the Model 6 unadjusted analysis exhibited only two significant results. However, after adjustment for covariates, no positive significant associations were found from the adjusted analyses of Models 4, 5, and 6.

Each model analyses produced a smaller number of significant results from the adjusted analyses than from the unadjusted analyses due to the adjustment for important confounding effects such as education and occupation.

In conclusion, the differences in the Ranch Hand and Comparison groups, but the lack of an effect attributable to dioxin, suggest that factors other than dioxin exposure continue to contribute to a relatively small but notable number of Ranch Hand test score abnormalities. Ranch Hands with psychological make-ups predisposing them to higher levels of anxiety, psychophysiological disturbances, and related somatic concerns, resulting from repeated public suggestion of physical and psychological consequences of dioxin exposure, would predictably demonstrate a self-perpetuating pattern of either static or escalating physical and psychological symptoms. Previous studies in clinical medicine continue to indicate the need for caution when interpreting the outcome of large statistical studies. The possibility that a small subset of physically or psychologically vulnerable Ranch Hands may have suffered psychological injury in the context of their exposure to dioxin cannot be definitively ruled out at this time.

CHAPTER 12
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CHAPTER 13

GASTROINTESTINAL ASSESSMENT

INTRODUCTION

Background

In contrast with the wealth of dioxin research data available in animal models, there is relatively little information about the effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD, or dioxin) on the human digestive system. Although the pharmacokinetics of orally ingested TCDD in a human volunteer have been reported (1), the pathologic lesions that have been studied in animals (gastric metaplasia with ulceration and ileitis) have not been described in human populations, in which the principal route of exposure has been transcutaneous. Further, in two reports of extreme phenoxyherbicide toxicity by ingestion in three humans, the primary target organs were the central nervous system with associated coma, and the musculoskeletal system with rhabdomyolysis and renal failure, rather than digestive system effects (2,3).

The digestive system and the liver have been clearly defined as target organs for TCDD toxicity in numerous laboratory and domestic animals (4-9). TCDD ingested by rodents (10-18) and adult monkeys (19) is absorbed by the intestinal lymphatics, transported by chylomicrons in enterohepatic circulation, and preferentially stored in the liver. Hepatotoxic manifestations, which appear to be dose- and time-dependent, include cellular hypertrophy, parenchymal necrosis (principally centrilobular), and fatty degeneration (9, 20-21).

Much of the basic animal research into the mechanism of TCDD-induced hepatotoxicity has focused on the definition and function of the aryl hydrocarbon (Ah) receptor, a stereospecific protein present in the cytosol of hepatic parenchymal cells in some animal species (22-27). Capable of binding aromatic hydrocarbons, the species- and strain-specific Ah receptor mediates a broad range of biochemical and enzymatic reactions, many of which are dependent on the ferrocytochrome P-450 enzyme system (22,28-31). In rats, TCDD administration is associated with increased gastrin secretion (32) and hypertrophy of the gastric antral mucosa (33). This Ah receptor has not been identified in humans.

A host of hepatic biochemical reactions related to TCDD toxicity have been studied including enhanced lipid peroxidation (10, 34-39), hepatic prostaglandin synthetase activity (40), and inhibition of glutathione peroxidase (36). Results from several lines of biochemical investigation have created a bridge between animal and human studies including research into lipid (39,41-44) and porphyrin metabolism (45-48). In rats, TCDD has been shown to increase the activity of glucuronyl transferase (49), which has led in turn to the use of urinary d-glucaric acid as a marker for TCDD exposure in some human epidemiologic studies (50-52).

Numerous human morbidity studies from the industrial sector have reported abnormal indices of liver function in most cases unassociated with any other clinical evidence for

hepatic or gastrointestinal disease (53-57). Further, in longer-term followup studies, abnormalities noted at the time of acute exposure appeared to disappear over time (58-62).

Several reports of Vietnam veterans have focused on the potential association of hepatic and digestive diseases with Herbicide Orange exposure. In one retrospective cohort study, in which the self-reporting of a rash during or after duty in Vietnam was used as a surrogate for dioxin exposure, an increased prevalence of liver enzyme abnormalities was noted but attributed to prior viral hepatitis and alcohol consumption (63). Similarly, chronic alcoholism contributed to increased mortality from digestive diseases (cirrhosis and peptic ulcer) in a study of U.S. Army Chemical Corps veterans (64).

Few epidemiologic studies have correlated tissue dioxin levels with indices of the digestive system. One report, employing adipose samples assayed for TCDD, found no abnormalities in standard tests of liver function related to the body burden of dioxin (65).

The National Institutes for Occupational Safety and Health (NIOSH) is conducting a comprehensive cross-sectional study of industrial workers proved by serum TCDD levels to have had significant occupational exposure to dioxin. In a recent report comparing 281 exposed (mean lipid-adjusted serum TCDD level of 220 pg per gram of lipid) and 260 controls (mean serum TCDD of 7 pg per gram of lipid) there was no evidence for an increased risk of clinical hepatic or gastrointestinal disease related to dioxin exposure. Upon further analysis, a statistically significant elevation in gamma glutamyl transferase (GGT) in the exposed group was attributed to alcohol consumption (66).

Finally, in the most recent reports of the Air Force Health Study (AFHS), the latest of which includes serum dioxin data (67,68), there was no increase in the prevalence of hepatic or digestive disease in the Ranch Hand cohort versus the Comparisons.

Summary of Previous Analyses of the Air Force Health Study

1982 Baseline Study Summary Results

The 1982 AFHS examination included an extensive evaluation of hepatic status by questionnaire, physical examination, and laboratory testing. The questionnaire elicited data on liver conditions, liver disease, and symptoms compatible with porphyria cutanea tarda (PCT), as well as detailed information on PCT risk factors (e.g., alcohol consumption, chemical exposures). The physical examination measured hepatomegaly, or enlarged liver, when present and determined liver function and porphyrin patterns by a comprehensive battery of 12 laboratory tests.

The questionnaire showed that Ranch Hands reported more miscellaneous liver conditions (verified by medical record reviews) and more skin changes compatible with PCT than their Comparisons. Although the reported skin changes were statistically significant, no cases of PCT were diagnosed at examination in either cohort.

Ranch Hands had slightly higher GGT and lactic dehydrogenase (LDH) results and lower cholesterol levels; no differences were found for bilirubin or alkaline phosphatase

levels. All of these two-factor interactions were statistically significant ($p<0.05$). There were no significant group differences in uroporphyrin, coproporphyrin, or d-aminolevulinic acid levels, nor did any test set support a diagnosis of PCT.

The comprehensive hepatic evaluation did not reveal any consistent pattern of significant liver damage in the Ranch Hand group.

1985 Followup Study Summary Results

The 1985 AFHS examination continued the emphasis on hepatic function and expanded the porphyrin test battery to six assays. The interval questionnaire revealed sparse reporting of liver disorders from 1982 to 1985. Reported liver diseases were verified by medical records, and these data were added to the verified Baseline history to assess possible lifetime differences. No significant differences were found.

The physical examination disclosed a marginally significant increase of hepatomegaly in the Ranch Hand group. Emphasis was placed on nine laboratory test variables measuring liver functions—aspartate aminotransferase (AST), alanine aminotransferase (ALT, previously called serum glutamic-pyruvic transaminase or SGPT), GGT, alkaline phosphatase, total and direct bilirubin, LDH, cholesterol, triglycerides—additionally, uroporphyrin and coproporphyrin measurements were obtained to assess the likelihood of PCT.

Only four variables produced differences of any note. The results showed a significantly lower mean ALT level, a greater mean alkaline phosphatase level, a lower mean uroporphyrin level, and a marginally significant greater mean coproporphyrin level in Ranch Hands. Only for alkaline phosphatase was the discrete analysis statistically significant.

Overall, the followup examination laboratory data showed no adverse clinical or exposure patterns in either group. Further, highlighting the difference between statistical significance and biological relevance, the continuous statistical tests detected significant mean shifts (still within normal range) that were not mirrored by the discrete tests. These findings were generally consistent with the 1982 Baseline data. Slight differences in analytic results are probably due to the use of more fully adjusted models for the 1985 followup examination data.

Interval reporting of PCT-like symptoms of skin patches, bruises, and sensitivity was significantly increased in Ranch Hands. However, when these historic data were contrasted to both uroporphyrin and coproporphyrin abnormalities, no correlation was apparent, nor were there any significant group differences. The likelihood of bona fide PCT among study participants, and particularly among the Ranch Hands, appears to be remote.

1987 Followup Study Summary Results

Overall, the gastrointestinal assessment did not find the health of the Ranch Hand group to be significantly different from that of the Comparison group. Group differences based on verified historical data from the questionnaire were not significant for eight categories of liver disease. No significant group difference was found for past or present occurrence of

peptic ulcers. The prevalence of hepatomegaly diagnosed at the physical examination also was not significantly different between the two groups. The only significant finding from the laboratory examination variables was that Ranch Hands had a higher mean alkaline phosphatase than Comparisons, also noted at the 1985 examination. Group differences for the other laboratory variables (AST, ALT, GGT, total bilirubin, direct bilirubin, LDH, cholesterol, high-density lipoprotein [HDL], cholesterol-HDL ratio, triglycerides, and creatine kinase) were not significant.

Serum Dioxin Analysis of 1987 Followup Study Summary Results

The 1987 serum dioxin analyses did not show a significant association with any of the verified historical liver disorder variables. However, the analyses of the laboratory variables detected significant associations between dioxin (current and estimated initial) and lipid-related health indices such as cholesterol, HDL cholesterol, the cholesterol-HDL ratio, and triglycerides. These findings were consistent with significant associations seen for fat-related variables in other clinical assessments such as the percent body fat results in the General Health Assessment and the diabetes and glucose results noted in the Endocrine Assessment, and may represent a dioxin mediated alteration of biochemical processes.

Parameters for the Gastrointestinal Assessment

Dependent Variables

Questionnaire, physical examination, and laboratory data were used in the gastrointestinal assessment. The questionnaire data was organized by International Classification of Diseases, 9th Edition, Clinical Modification (ICD-9-CM) medical coding categories.

Medical Records Data

During the 1992 health interview, each study participant was asked about the occurrence of hepatitis, jaundice, cirrhosis, enlarged liver, and other liver conditions. This self-reported information was captured in the questionnaire and combined with information from the Baseline, 1985, and 1987 examinations and verified by medical record review. The verified results were grouped into eight categories of disorders for analysis: hepatitis (non-A, non-B, and non-C), jaundice (unspecified, not of the newborn), acute and subacute necrosis of the liver, chronic liver disease and cirrhosis (alcohol-related and nonalcohol-related cirrhosis will be analyzed separately), liver abscess and sequelae of chronic liver disease, other disorders of the liver (ICD codes 5730-5739, 7901, 7904, 7905, and 7948), and enlarged liver (hepatomegaly). Hepatitis (non-A, non-B, and non-C) was verified by serological testing. The purpose of the hepatitis (non-A, non-B, and non-C) category was to define a category that was neither clearly A nor B nor C, so that liver disease misdiagnosed as "viral hepatitis" could be detected. This approach to historical hepatitis creates a group of cases that could have been chemically induced. The category of other liver disorders includes elevated enzyme elevations as well as conditions such as abnormal liver scans, unspecified liver disorders, and unspecified hepatitis. The majority of AFHS participants with a medical history of other liver disorders were individuals who had been told at a previous AFHS

examination that they had a nonspecific elevation of a laboratory test (687/691). Only four participants had an actual diagnosed liver disease. Abnormal enzyme elevations and unspecified hepatitis also are in this category.

Information on the occurrence of skin bruises, patches, and sensitivity also was captured in all four questionnaires (1982, 1985, 1987, and 1992). The occurrence of skin bruises, patches, and sensitivity was intended to be a surrogate measure for symptoms of PCT. However, the diagnoses of the individuals reporting "yes" to skin bruises, patches, or sensitivity included such a broad range of conditions that meaningful analysis was not feasible. Appendix Table I-1-1 displays the diagnoses for all of the participants who reported "yes" to skin bruises, patches, or sensitivity.

For each condition, participants with a pre-SEA diagnosis were excluded from the analysis.

Physical Examination Data

One variable from the 1992 physical examination, current hepatomegaly, was analyzed in the gastrointestinal assessment. This variable was coded as "yes" or "no." Participants whose blood contained hepatitis B surface antigen (HB_sAg) or hepatitis C antibodies were excluded from the analysis of current hepatomegaly to account for the effects of these viruses on chronic hepatic disease.

Laboratory Examination Data

The 1992 examination emphasized the evaluation of laboratory data through the analysis of 28 measurements. Twelve of these laboratory variables were common to the statistical analysis for the 1987 examination: AST (U/L), ALT (U/L), GGT (U/L), alkaline phosphatase (U/L), total bilirubin (mg/dl), direct bilirubin (mg/dl), lactic dehydrogenase (LDH in U/L), cholesterol (mg/dl), high-density lipoproteins (HDL in mg/dl), cholesterol-HDL ratio, triglycerides (mg/dl), and creatine kinase (U/L). In addition, the 1992 gastrointestinal assessment was expanded to include serum amylase (U/L), antibodies for hepatitis A, serological evidence of prior hepatitis B infection, antibodies for hepatitis C, stool hemoccult, and 10 components (in mg/dl) in a protein profile (prealbumin, albumin, α-1-acid glycoprotein, α-1-antitrypsin, α-2-macroglobulin, apolipoprotein B, C_3 complement, C_4 complement, haptoglobin, and transferrin). IgA, IgG, and IgM also were part of this profile, but they were analyzed in the Immunologic Assessment (see Chapter 19).

Baxter/Dade Paramax® equipment was used to quantify the 12 laboratory variables analyzed previously as well as serum amylase (added in 1992). The Brooks Air Force Base (AFB), Texas, laboratory determined antibodies of hepatitis A, serological evidence of present or prior hepatitis B infection: hepatitis B surface antigen (HB_sAg) and its antibody, anti-HB_s; anti-hepatitis B core antibodies (IgM anti-HB_c and IgG anti-HB_c); hepatitis B_e antigen (HB_eAg) and its antibody, anti-HB_e, and antibodies of hepatitis C. The Beckman Array Protein System® quantified the components of the protein profile.

All laboratory variables were analyzed in both continuous and discrete forms except for direct bilirubin, antibodies for hepatitis A, positive serological evidence of present or prior hepatitis B infection, antibodies for hepatitis C, and stool hemoccult, which were analyzed only in discrete form. The continuous data were transformed to enhance normality, if necessary. Direct bilirubin was analyzed only in its discrete form because there were few distinct measurements, precluding a meaningful continuous analysis.

Participants whose blood contained HB_sAg or hepatitis C antibodies, and participants with body temperatures greater than or equal to 100° Fahrenheit, were excluded from the analysis of all laboratory variables except antibodies for hepatitis A, serological evidence of prior hepatitis B infection, and antibodies for hepatitis C. For these three hepatitis variables, no participants were excluded.

One Ranch Hand was found to have a history of hepatitis C after the statistical analyses for hepatitis C were well underway. Consequently, the analyses of the dependent variable "Antibodies for Hepatitis C" were changed to include this individual, but the exclusion category "Presence of Hepatitis C Antibodies" was not modified. This Ranch Hand did not have a dioxin measurement and therefore only the results of Model 1 were affected.

Covariates

Race, military occupation, lifetime alcohol history, lifetime industrial chemical exposure, and lifetime degreasing chemical exposure were candidate covariates in the adjusted analyses for all of the medical records variables. Similar to the 1987 gastrointestinal serum dioxin analysis, the adjusted analyses for all of the medical records variables retained age because older individuals are more susceptible to disease than younger individuals and therefore may tend to have a higher historical occurrence of disease. Also, the analysis of chronic liver disease and cirrhosis (alcohol-related) excluded participants with zero lifetime alcohol history because nondrinkers would not be at risk for alcohol-related liver disease.

Age, race, military occupation, current alcohol use, lifetime alcohol history, lifetime industrial chemical exposure, and lifetime degreasing chemical exposure were candidate covariates for the adjusted analyses of the physical examination variable and all of the laboratory variables except alkaline phosphatase, antitrypsin, antibodies for hepatitis A, serological evidence of prior hepatitis B infection, and antibodies for hepatitis C. The adjusted analyses for antibodies for hepatitis A, serological evidence of prior hepatitis B infection, and antibodies for hepatitis C used all of the candidate covariates except current alcohol use. Wine use showed a strong negative association with alkaline phosphatase in the 1985 and 1987 examinations. The negative association persisted in the 1992 followup data; therefore, current wine use and lifetime wine history replaced current alcohol use and lifetime alcohol history as candidate covariates for alkaline phosphatase. Current wine consumption replaced current alcohol use in the adjusted analysis of α-1 antitrypsin because covariate associations of the 1992 followup data showed that antitrypsin was highly associated with current wine use, but not associated with current alcohol use.

The lifetime alcohol (or wine) history and current alcohol (or wine) use covariates were based on self-reported information from the questionnaire. For lifetime alcohol history, the respondent's average daily alcohol consumption was determined for various drinking stages throughout his lifetime, and an estimate was derived for the corresponding total number of drink-years (1 drink-year is the equivalent of drinking 1.5 ounces of 80-proof alcoholic beverage per day for 1 year). The current alcohol use covariate was based on average daily alcohol consumption for the month prior to completing the questionnaire. Exposure to industrial chemicals and degreasing chemicals covariates represented lifetime exposure based on self-reported questionnaire data.

Age, current alcohol use, and lifetime alcohol history were treated as continuous variables for all adjusted analyses and were categorized to explore interactions. Current wine use and lifetime wine history were treated as continuous variables for the adjusted alkaline phosphatase analyses and were categorized for interaction exploration. For α-1 antitrypsin, the adjusted analysis also treated current wine use as a continuous variable and categorized it to study interactions. Degreasing chemical exposure and industrial chemical exposure were categorized as yes or no for all analyses.

Statistical Methods

Table 13-1 summarizes the statistical analyses performed for the gastrointestinal assessment. The basic statistical analysis methods used are described in Chapter 7, Statistical Methods. The first part of Table 13-1 lists the dependent variables analyzed, the source of the data, the form of the data (discrete or continuous), the cutpoints, the candidate covariates, and the statistical methods. The second part of this table provides a further description of the candidate covariates examined. Abbreviations used in the body of the table are defined at the end of the table.

Table 13-2 provides the number of participants with missing dependent variable and covariate data, and the number of participants excluded for medical reasons and pre-SEA-conditions.

Cutpoints for cholesterol, HDL cholesterol, and triglycerides are age-dependent. Consequently, normal and abnormal levels were constructed according to a participant's laboratory value and age at the physical examination. The age-specific cutpoints are listed in Table 13-1, and the reference ages for these cutpoints are given in parentheses following the cutpoints.

Analyses of data collected at the 1987 followup study indicated that dioxin was associated with military occupation. In general, enlisted personnel had higher levels of dioxin than officers, with enlisted groundcrew having higher levels than enlisted flyers. Consequently, adjustment for military occupation in statistical models using dioxin as a measure of exposure may improperly mask an actual dioxin effect. However, occupation also can be a surrogate for socioeconomic effects. Failure to adjust for occupation could overlook important risk factors related to lifestyle. If occupation was found to be significantly associated with a dependent variable in the 1992 followup analyses and was

Table 13-1.
Statistical Analyses for the Gastrointestinal Assessment

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analyses
Hepatitis (Non-A, Non-B, and Non-C)	MR-V	D	Yes No	AGE,RACE, OCC,DRKYR, IC,DC	U:LR,CS A:LR
Jaundice (Unspecified)	MR-V	D	Yes No	AGE,RACE, OCC,DRKYR, IC,DC	U:LR,CS A:LR
Acute and Subacute Necrosis of the Liver	MR-V	D	Yes No	--	Frequencies
Chronic Liver Disease and Cirrhosis (Alcohol-Related)	MR-V	D	Yes No	AGE,RACE, OCC,DRKYR, IC,DC	U:LR,CS A:LR
Chronic Liver Disease and Cirrhosis (Nonalcohol-Related)	MR-V	D	Yes No	AGE,RACE, OCC,DRKYR, IC,DC	U:LR,CS A:LR
Liver Abscess and Sequelae of Chronic Liver Disease	MR-V	D	Yes No	--	Frequencies
Other Liver Disorders	MR-V	D	Yes No	AGE,RACE, OCC,DRKYR, IC,DC	U:LR,CS A:LR
Hepatomegaly	MR-V	D	Yes No	AGE,RACE, OCC,DRKYR, IC,DC	U:LR,CS A:LR
Current Hepatomegaly	PE	D	Yes No	AGE,RACE, OCC,ALC, DRKYR,IC,DC	U:LR,CS A:LR
AST (U/L)	LAB	D/C	High: >50 Normal: ≤ 50	AGE,RACE, OCC,ALC, DRKYR,IC,DC	U:LR,CS,GLM, TT A:LR,GLM L:LR,GLM

Table 13-1. (Continued)
Statistical Analyses for the Gastrointestinal Assessment

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analyses
ALT (U/L)	LAB	D/C	High: >55 Normal: ≤55	AGE,RACE, OCC,ALC, DRKYR,IC,DC	U:LR,CS,GLM, TT A:LR,GLM L:LR,GLM
GGT (U/L)	LAB	D/C	High: >51 Normal: ≤51	AGE,RACE, OCC,ALC, DRKYR,IC,DC	U:LR,CS,GLM, TT A:LR,GLM L:LR,GLM
Alkaline Phosphatase (U/L)	LAB	D/C	High: >107 Normal: ≤107	AGE,RACE, OCC,WINE, LWINE,IC,DC	U:LR,CS,GLM, TT A:LR,GLM
Total Bilirubin (mg/dl)	LAB	D/C	High: >1.2 Normal: ≤1.2	AGE,RACE, OCC,ALC, DRKYR,IC,DC	U:LR,CS,GLM, TT A:LR,GLM
Direct Bilirubin (mg/dl)	LAB	D	High: >0.4 Normal: ≤0.4	AGE,RACE, OCC,ALC, DRKYR,IC,DC	U:LR,CS A:LR
Lactic Dehydrogenase (LDH) (U/L)	LAB	D/C	High: >172 Normal: ≤172	AGE,RACE, OCC,ALC, DRKYR,IC,DC	U:LR,CS,GLM, TT A:LR,GLM
Cholesterol (mg/dl)	LAB	D/C	High: >250 (40-44) >260 (45-69) >250 (≥70) Normal: ≤250 (40-44) ≤260 (45-69) ≤250 (≥70)	AGE,RACE, OCC,ALC, DRKYR,IC,DC	U:LR,CS,GLM, TT A:LR,GLM L:LR,GLM
HDL Cholesterol (mg/dl)	LAB	D/C	Low: <25 (40-44) <30 (≥45) Normal: ≥25 (40-44) ≥30 (≥45)	AGE,RACE, OCC,ALC, DRKYR,IC,DC	U:LR,CS,GLM, TT A:LR,GLM L:LR,GLM

Table 13-1. (Continued)
Statistical Analyses for the Gastrointestinal Assessment

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analyses
Cholesterol-HDL Ratio	LAB	D/C	High: >5 Normal: ≤5	AGE,RACE, OCC,ALC, DRKYR,IC,DC	U:LR,CS,GLM, TT A:LR,GLM L:LR,GLM
Triglycerides (mg/dl)	LAB	D/C	High: >320 (40-54) >290 (55-64) >260 (≥65) Normal: ≤320 (40-54) ≤290 (55-64) ≤260 (≥65)	AGE,RACE, OCC,ALC, DRKYR,IC,DC	U:LR,CS,GLM, TT A:LR,GLM L:LR,GLM
Creatine Kinase (U/L)	LAB	D/C	High: >224 Normal: ≤224	AGE,RACE, OCC,ALC, DRKYR,IC,DC	U:LR,CS,GLM, TT A:LR,GLM
Serum Amylase (U/L)	LAB	D/C	High: >122 Normal: ≤122	AGE,RACE, OCC,ALC, DRKYR,IC,DC	U:LR,CS,GLM, TT A:LR,GLM
Antibodies for Hepatitis A	LAB-AF	D	Yes No	AGE,RACE, OCC,DRKYR, IC,DC	U:LR,CS A:LR
Serological Evidence of Present or Prior Hepatitis B Infection	LAB-AF	D	Yes No	AGE,RACE, OCC,DRKYR, IC,DC	U:LR,CS A:LR
Antibodies for Hepatitis C	LAB-AF	D	Yes No	AGE,RACE, OCC,DRKYR, IC,DC	U:LR,CS A:LR
Stool Hemoccult	LAB	D	Yes No	AGE,RACE, OCC,ALC, DRKYR,IC,DC	U:LR,CS A:LR
Protein Profile: Prealbumin (mg/dl)	LAB	D/C	Low: <17 Normal: ≥17	AGE,RACE, OCC,ALC, DRKYR,IC,DC	U:LR,CS,GLM, TT A:LR,GLM

Table 13-1. (Continued)
Statistical Analyses for the Gastrointestinal Assessment

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analyses
Protein Profile: Albumin (mg/dl)	LAB	D/C	Low: <3,350 Normal: ≥3,350	AGE,RACE, OCC,ALC, DRKYR,IC,DC	U:LR,CS,GLM, TT A:LR,GLM
Protein Profile: α-1 Acid Glycoprotein (mg/dl)	LAB	D/C	High: >88 Normal: ≤88	AGE,RACE, OCC,ALC, DRKYR,IC,DC	U:LR,CS,GLM, TT A:LR,GLM
Protein Profile: α-1 Antitrypsin (mg/dl)	LAB	D/C	Abnormal Low: <93 Normal: 93-224 Abnormal High: >224	AGE,RACE, OCC,WINE, DRKYR,IC,DC	U:PR,CS,GLM, TT A:PR,GLM
Protein Profile: α-2 Macroglobulin (mg/dl)	LAB	D/C	High: >269 Normal: ≤269	AGE,RACE, OCC,ALC, DRKYR,IC,DC	U:LR,CS,GLM, TT A:LR,GLM
Protein Profile: Apolipoprotein B (mg/dl)	LAB	D/C	High: >128 Normal: ≤128	AGE,RACE, OCC,ALC, DRKYR,IC,DC	U:LR,CS,GLM, TT A:LR,GLM
Protein Profile: C_3 Complement (mg/dl)	LAB	D/C	Low: <85 Normal: ≥85	AGE,RACE, OCC,ALC, DRKYR,IC,DC	U:LR,CS,GLM, TT A:LR,GLM
Protein Profile: C_4 Complement (mg/dl)	LAB	D/C	Low: <12 Normal: ≥12	AGE,RACE, OCC,ALC, DRKYR,IC,DC	U:LR,CS,GLM, TT A:LR,GLM
Protein Profile: Haptoglobin (mg/dl)	LAB	D/C	High: >163 Normal: ≤163	AGE,RACE, OCC,ALC, DRKYR,IC,DC	U:LR,CS,GLM, TT A:LR,GLM
Protein Profile: Transferrin (mg/dl)	LAB	D/C	Low: <252 Normal: ≥252	AGE,RACE, OCC,ALC, DRKYR,IC,DC	U:LR,CS,GLM, TT A:LR,GLM

Table 13-1. (Continued)
Statistical Analyses for the Gastrointestinal Assessment

Covariates

Variable (Units)	Data Source	Data Form	Cutpoints
Age (AGE)	MIL	D/C	Born ≥1942 Born <1942
Race (RACE)	MIL	D	Black Non-Black
Occupation (OCC)	MIL	D	Officer Enlisted Flyer Enlisted Groundcrew
Industrial Chemical Exposure (IC)	Q-SR	D	Yes No
Degreasing Chemical Exposure (DC)	Q-SR	D	Yes No
Current Alcohol Use (drinks/day) (ALC)	Q-SR	D/C	0-1 >1-4 >4
Lifetime Alcohol History (drink-years) (DRKYR)	Q-SR	D/C	0 >0-40 >40
Current Wine Use (drinks of wine/day) (WINE)	Q-SR	D/C	0 >0
Lifetime Wine History (drink-years of wine) (LWINE)	Q-SR	D/C	0 >0

Table 13-1. (Continued)
Statistical Analyses for the Gastrointestinal Assessment

Abbreviations

Data Source:	LAB	= 1992 laboratory results
	LAB-AF	= 1992 Brooks AFB laboratory results
	MIL	= Air Force military records
	MR-V	= Medical records (verified)
	PE	= 1992 physical examination
	Q-SR	= Health questionnaires (self-reported)
Data Form:	D	= Discrete analysis only
	D/C	= Discrete and continuous analyses for dependent variables; appropriate form for analysis (either discrete or continuous) for covariates
Statistical Analyses:	U	= Unadjusted analyses
	A	= Adjusted analyses
	L	= Longitudinal analyses
Statistical Methods:	CS	= Chi-square contingency table analysis (continuity-adjusted for 2x2 tables)
	GLM	= General linear models analysis
	LR	= Logistic regression analysis
	PR	= Polytomous logistic regression analysis
	TT	= Two-sample t-test

Table 13-2.
Number of Participants with Missing Data for, or Excluded from, the Gastrointestinal Assessment

		Group		Dioxin (Ranch Hands Only)		Categorized Dioxin	
Variable	Variable Use	Ranch Hand	Comparison	Initial	Current	Ranch Hand	Comparison
Current Hepatomegaly	DEP	0	1	0	0	0	1
AST	DEP	0	1	0	0	0	0
ALT	DEP	0	1	0	0	0	0
GGT	DEP	0	1	0	0	0	0
Alkaline Phosphatase	DEP	0	1	0	0	0	0
Total Bilirubin	DEP	0	1	0	0	0	0
Direct Bilirubin	DEP	0	1	0	0	0	0
LDH	DEP	1	2	0	0	0	1
Cholesterol	DEP	0	1	0	0	0	0
HDL Cholesterol	DEP	14	13	9	13	13	10
Cholesterol-HDL Ratio	DEP	14	13	9	13	13	10
Triglycerides	DEP	0	1	0	0	0	0
Creatine Kinase	DEP	0	1	0	0	0	0
Serum Amylase	DEP	0	1	0	0	0	0
Antibodies for Hepatitis A	DEP	0	1	0	0	0	0
Serological Evidence of Prior Hepatitis B Infection	DEP	0	1	0	0	0	0
Antibodies for Hepatitis C	DEP	0	1	0	0	0	0
Stool Hemoccult	DEP	43	55	26	37	37	39
Prealbumin	DEP	0	1	0	0	0	0
Albumin	DEP	0	1	0	0	0	0
α-1 Acid Glycoprotein	DEP	0	1	0	0	0	0
α-1 Antitrypsin	DEP	0	1	0	0	0	0
α-2 Macroglobulin	DEP	0	1	0	0	0	0
Apolipoprotein B	DEP	0	1	0	0	0	0

Table 13-2. (Continued)
Number of Participants with Missing Data for, or Excluded from, the Gastrointestinal Assessment

		Group		Dioxin (Ranch Hands Only)		Categorized Dioxin	
Variable	Variable Use	Ranch Hand	Comparison	Initial	Current	Ranch Hand	Comparison
C_3 Complement	DEP	0	1	0	0	0	0
C_4 Complement	DEP	0	1	0	0	0	0
Haptoglobin	DEP	0	1	0	0	0	0
Transferrin	DEP	0	1	0	0	0	0
Current Alcohol Use	COV	10	18	7	9	9	16
Lifetime Alcohol History	COV	22	21	13	20	20	18
Current Wine Use	COV	11	18	7	10	10	16
Lifetime Wine History	COV	19	21	11	17	17	18
Pre-SEA Hepatitis (Non-A, Non-B, or Non-C)	EXC	8	9	4	8	8	8
Pre-SEA Jaundice (Unspecified)	EXC	24	33	13	24	24	28
Pre-SEA Acute and Subacute Necrosis of the Liver	EXC	0	1	0	0	0	1
Pre-SEA Chronic Liver Disease and Cirrhosis (Alcohol-Related)	EXC	1	4	1	1	1	4
Pre-SEA Chronic Liver Disease and Cirrhosis (Nonalcohol-Related)	EXC	0	1	0	0	0	1
Pre-SEA Other Liver Disorders	EXC	4	11	1	4	4	10
Pre-SEA History of Hepatomegaly	EXC	1	2	1	1	1	2
Hepatitis B Surface Antigen	EXC	4	3	3	4	4	3

Table 13-2. (Continued)
Number of Participants with Missing Data for, or Excluded from, the Gastrointestinal Assessment

		Group		Dioxin (Ranch Hands Only)		Categorized Dioxin	
Variable	Variable Use	Ranch Hand	Comparison	Initial	Current	Ranch Hand	Comparison
Presence of Hepatitis C Antibodies	EXC	7	23	2	4	4	16
Fever	EXC	3	1	1	3	3	1

Abbreviations: DEP = Dependent variable (missing data).
COV = Covariate (missing data).
EXC = Exclusion.

Note: 952 Ranch Hands and 1,281 Comparisons;
520 Ranch Hands for initial dioxin; 894 Ranch Hands for current dioxin;
894 Ranch Hands and 1,063 Comparisons for categorized dioxin.
One Ranch Hand missing total lipids for current dioxin.

retained in the final statistical models using dioxin as a measure of exposure, the dioxin effect was evaluated in the context of two models. Analyses were performed with and without occupation in the final models to investigate whether conclusions regarding the association between the health endpoint and dioxin differed.

The results of the analyses without occupation are presented in Appendix I-3 and are only discussed in the text if the level of significance differs from the original final adjusted model (significant versus nonsignificant).

Longitudinal Analysis

The longitudinal analyses of the gastrointestinal assessment examined seven laboratory variables (AST, ALT, GGT, cholesterol, HDL cholesterol, the cholesterol-HDL ratio, and triglycerides). Each variable was analyzed in both continuous and discrete forms. AST, ALT, and GGT were analyzed longitudinally in previous phases of the AFHS; the other variables were added to the 1992 analyses because they all showed significant associations with dioxin in the previous serum dioxin analyses. These longitudinal analyses were used to assess any relationship between dioxin and hepatic changes across time.

RESULTS

Dependent Variable-Covariate Associations

Covariate tests of association were done to examine the unadjusted relationships between the covariates used in the adjusted analyses and the dependent variables. Appendix Table I-1-2 provides summary results of these analyses, including correlation coefficients (r), percents abnormal, means, and p-values to test the statistical significance of the association. Statistically significant associations are discussed below.

Age

For the historical liver disorder variables, age exhibited a significant positive association with hepatomegaly. The prevalence of hepatomegaly was lower for younger participants than for older participants (1.3% for men born in or after 1942 vs. 3.0% for men born before 1942, $p=0.010$). The covariate tests of association did not find age to be significantly associated with the other historical variables.

For the laboratory variables, age was negatively correlated with ALT ($r=-0.141$, $p<0.001$) and creatine kinase ($r=-0.093$, $p<0.001$) and positively correlated with alkaline phosphatase ($r=0.047$, $p=0.029$), LDH ($r=0.084$, $p<0.001$), and serum amylase ($r=0.060$, $p=0.005$). Analyses of the discretized form of these dependent variables showed similar results. Older participants were more likely to have antibodies for hepatitis A than younger participants (42.0% vs. 22.8%, $p<0.001$), probably reflecting the cumulative risk of exposure with advancing age.

Age was significantly correlated with many of the protein profile variables, including negative correlations with prealbumin ($r=-0.143$, $p<0.001$), albumin ($r=-0.161$, $p<0.001$),

and transferrin ($r=-0.054$, $p=0.011$), as well as positive associations with α-1 antitrypsin ($r=0.152$, $p<0.001$), α-2 macroglobulin ($r=0.251$, $p<0.001$), apolipoprotein B ($r=0.047$, $p=0.027$), and haptoglobin ($r=0.094$, $p<0.001$). Analyses of the discretized form of these dependent variables showed similar results.

Race

Race was a significant factor in the prevalence of other liver disorders. Black participants were much more likely than non-Black participants to have a medical history of other liver disorders (47.3% vs. 27.6%, $p<0.001$). There were no significant racial differences for the other historical variables.

For the hepatic enzymes, Blacks had a significantly higher mean level of GGT ($p=0.005$) and significantly more abnormal high LDH levels ($p=0.040$) than non-Blacks. Of the lipid and carbohydrate indices, Blacks had a significantly higher mean level of HDL cholesterol ($p<0.001$) and fewer abnormal low values ($p=0.047$) than non-Blacks. Blacks also had significantly lower mean levels of triglycerides ($p<0.001$) and a lower mean cholesterol-HDL ratio ($p=0.001$), as well as a significantly lower prevalence of abnormalities for both of these variables.

The creatine kinase mean was much higher for Blacks than for non-Blacks (233.07 mg/dl vs. 124.27 mg/dl, $p<0.001$) as was the percentage of abnormal high levels (51.6% vs. 11.7%, $p<0.001$). These findings also were noted at previous examinations. Blacks had a significantly higher mean level of serum amylase ($p<0.001$) and more than three times as many abnormal high values as did non-Blacks.

Blacks had a significantly higher history of antibodies for hepatitis A and C ($p=0.007$ and $p=0.039$ respectively) and a significantly higher history of serological evidence of prior hepatitis B infection ($p<0.001$) than did non-Blacks.

Of the protein profile variables, Blacks had significantly lower mean levels of albumin, ($p=0.019$) and α-2 macroglobulin ($p<0.001$), and significantly higher mean levels of C_3 complement ($p<0.001$) and C_4 complement ($p<0.001$) than did non-Blacks. However, the corresponding discrete analyses for these variables did not show that the prevalence of abnormal levels differed significantly between Blacks and non-Blacks. The mean level of transferrin was significantly lower ($p=0.003$) and the percentage of abnormal low levels of transferrin was significantly higher ($p=0.006$) for Blacks.

Occupation

The covariate tests of association did not show significant occupational differences for any of the historical variables. By contrast, the mean levels or percent abnormal differed significantly among military occupations for most of the laboratory variables. In many instances, the mean levels or percent abnormal levels differed between the officer cohort and the enlisted cohorts, but in some cases there were differences between the enlisted flyers and the enlisted groundcrew, as in the tests of creatine kinase and stool hemoccult.

Industrial Chemical Exposure

None of the historical variables were significantly associated with industrial chemical exposure. But, for the laboratory variables, participants who had been exposed to industrial chemicals had significantly higher mean levels of the cholesterol-HDL ratio ($p=0.013$), triglycerides ($p=0.035$), α-1 acid glycoprotein ($p=0.032$), α-1 antitrypsin ($p=0.005$), C_3 complement ($p=0.002$), C_4 complement ($p=0.015$) and haptoglobin ($p=0.045$), and a lower mean level of HDL cholesterol than participants who had never been exposed to industrial chemicals ($p=0.031$). For each of those variables, other than the cholesterol-HDL ratio, the percentages of abnormalities did not differ significantly between exposed and non-exposed individuals. A greater number of participants exposed to industrial chemicals also had high cholesterol levels ($p=0.019$) and serological evidence of prior hepatitis B infection ($p=0.015$) than non-exposed participants.

Degreasing Chemical Exposure

The covariate tests of association results for degreasing chemical exposure found significant results for many of the same variables associated significantly with industrial chemical exposure. Similar to the industrial chemical exposure findings, participants exposed to degreasing chemicals had significantly higher mean levels of the cholesterol-HDL ratio ($p<0.001$), triglycerides ($p=0.018$), α-1 acid glycoprotein ($p=0.003$), α-1 antitrypsin ($p<0.001$), C_3 complement ($p<0.001$), and haptoglobin ($p<0.001$), and a lower mean HDL cholesterol level ($p=0.014$) than participants never exposed to degreasing chemicals. In addition, relatively more individuals exposed to degreasing chemicals had high cholesterol levels ($p=0.007$) and a history of serological evidence of prior hepatitis B infection ($p=0.009$) than non-exposed individuals. The degreasing chemical exposure results also showed that exposed participants had significantly higher mean ALT ($p=0.023$), cholesterol ($p=0.030$), apolipoprotein B ($p=0.015$), and transferrin ($p=0.001$) levels than non-exposed individuals.

Current Alcohol Use

The covariate tests of association found that current alcohol consumption correlated significantly with many of the laboratory variables. There were highly significant positive correlations with AST, ALT, GGT, total bilirubin, cholesterol, and HDL cholesterol, and a highly significant negative correlation with the cholesterol-HDL ratio ($p\leq0.001$ for each variable). The chi-square tests of association also were significant for the discrete forms of these variables as well as for direct bilirubin and LDH ($p\leq0.033$ for all analyses). In addition, there was a significant negative correlation with serum amylase ($p=0.032$).

Of the protein profile variables, current alcohol consumption was positively associated with prealbumin and α-1 acid glycoprotein in both the continuous and discrete analyses ($p\leq0.036$ for all analyses). There were also significant associations with α-1 antitrypsin (discrete only, $p=0.017$), C_3 complement (continuous only, a negative correlation, $p=0.018$), and haptoglobin (continuous only, a positive correlation, $p=0.007$).

Lifetime Alcohol History

The covariate tests of association results for lifetime alcohol history revealed expected significant positive relationships with alcohol-related chronic liver disease and cirrhosis ($p<0.001$), hepatomegaly ($p<0.001$), and the category of other liver disorders ($p=0.003$). In addition, the results for many of the laboratory variables also were significant, although some of these findings may be attributed to the interrelationship between lifetime alcohol history and current alcohol use. Significant positive associations were noted for AST, GGT, and HDL ($p \leq 0.002$ for all analyses), whereas significant decreasing associations were noted for the cholesterol-HDL ratio ($p<0.001$) and creatine kinase ($p=0.008$).

Participants with 0 drink-years had a higher history rate of antibodies for hepatitis A (41.0%) than participants with greater than 0 but less than 40 drink-years (32.1%) and those with greater than 40 drink-years (35.8%) ($p=0.046$). By contrast, 0 drink-year participants had the lowest rate of serological evidence of prior hepatitis B infection (11.2%) compared with the other lifetime alcohol history categories (12.4% for >0-40 drink-years, and 16.7% for >40 drink-years) ($p=0.030$). The history of antibodies for hepatitis C was not significantly associated with lifetime alcohol history.

There were several significant associations with the protein profile variables, including positive correlations with α-1 acid glycoprotein, α-1 antitrypsin, α-2 macroglobulin, and haptoglobin ($p \leq 0.004$ for all analyses). In addition, the percentage of abnormal low prealbumin levels increased with the number of drink-years ($p=0.005$).

Current Wine Use

Current wine use was used as an adjusting covariate instead of current alcohol use for alkaline phosphatase and α-1 antitrypsin because the covariate tests of association found significant decreasing associations ($p \leq 0.005$ for all analyses), whereas the results for current alcohol use were not significant. The alkaline phosphatase relationship was noted at previous examination cycles; α-1 antitrypsin had not been analyzed before.

Lifetime Wine History

Lifetime wine history was used as an adjusting covariate instead of lifetime alcohol history for alkaline phosphatase for the same reason current wine use was substituted for current alcohol use; the covariate tests of association found a significant decreasing association ($p=0.043$), whereas the results for lifetime alcohol history were not significant.

Exposure Analysis

The following section presents the results of the statistical analyses of the dependent variables shown in Table 13-1. Dependent variables are grouped into three sections: those derived and verified from a review of medical records, one variable obtained during the 1992 physical examination, and data derived from the laboratory portion of the 1992 followup examination.

Unadjusted and adjusted analyses of six models are presented for each variable. Model 1 examines the relationship between the dependent variable and group (Ranch Hand or Comparison). Model 2 explores the relationship between the dependent variable and an extrapolated initial dioxin measure for Ranch Hands who had a 1987 dioxin measurement greater than 10 ppt. If a participant did not have a 1987 dioxin level, a 1992 level was used. A statistical adjustment for the percent of body fat at the participant's time of duty in SEA and the change in the percent of body fat from the time of duty in SEA to the date of the blood draw for dioxin is included in this model to account for body-fat-related differences in elimination rate (69). Model 3 dichotomizes the Ranch Hands in Model 2 based on their initial dioxin measures; these two categories of Ranch Hands are referred to as the "low Ranch Hand" category and the "high Ranch Hand" category. These participants are added to Ranch Hands and Comparisons with current serum dioxin levels (1987, if available; 1992, if the 1987 level was not available) at or below 10 ppt to create a total of four categories. Ranch Hands with current serum dioxin levels at or below 10 ppt are referred to as the "background Ranch Hand" category. The relationship between the dependent variable in each of the three Ranch Hand categories and the dependent variable in the "Comparison" category is examined. A fourth contrast, exploring the relationship of the dependent variable in the low Ranch Hand category and the high Ranch Hand category combined, also is conducted. This combination is referred to in the text and tables as the "low plus high Ranch Hand" category. As in Model 2, a statistical adjustment is made for the percent of body fat at the participant's time of duty in SEA and the change in the percent of body fat from the time of duty in SEA to the date of the blood draw for dioxin.

Models 4, 5, and 6 examine the relationship between the dependent variable and 1987 dioxin levels in all Ranch Hands with a dioxin measurement. If a participant did not have a 1987 dioxin measurement, a 1992 measurement was utilized in determining the current dioxin level. The measure of dioxin in Model 4 is lipid-adjusted, whereas whole-weight dioxin is used in Models 5 and 6. Model 6 differs from Model 5 in that a statistical adjustment for total lipids is included in Model 6. Details on dioxin and the modeling strategy are found in Chapters 2 and 7 respectively.

The statistical significance of the results in Models 4, 5, and 6 may differ for cholesterol and other lipid variables because of the lipid-adjustment applied in Models 4 and 6. The whole-weight dioxin measure analyzed in Model 5 may be associated with the lipid variables because dioxin is lipophilic and correlates positively with lipid measures. The lipid-adjusted current dioxin level analyzed in Model 4 accounts for the correlation, which may result in less significant associations between TCDD and the lipid variables. The Model 6 analysis forces total lipids into the model as an adjusting covariate that often is highly associated with the lipid variables. The forced inclusion of total lipids into the model results in a higher R-squared and may cause the association between whole-weight TCDD and lipid variables to become nonsignificant.

Results of the investigation for group-by-covariate and dioxin-by-covariate interactions are referenced in the text, and tabular results are presented in Appendix I-2. As described previously, additional analyses were performed when occupation was retained in the final model for Models 2 through 6, Results excluding occupation from these models are tabled in Appendix I-3, and dioxin-by-covariate interactions with occupation excluded from these

models are presented in Appendix I-4. Results from analyses excluding occupation are discussed in the text only if a meaningful change occurred (that is, changes between significant results, marginally significant results, and nonsignificant results).

Verified Medical Records Variables

Hepatitis (Non-A, Non-B, and Non-C)

The unadjusted and adjusted Model 1 analyses of hepatitis did not find a significant difference between Ranch Hands and Comparisons (Table 13-3(a,b): $p>0.49$ for all contrasts). The adjusted model contained two covariate-by-covariate interactions: industrial chemical exposure-by-degreasing chemical exposure and age-by-industrial chemical exposure.

Similarly, the analyses of Models 2 and 3 did not show hepatitis to be significantly associated with initial dioxin or categorized dioxin (Tables 13-3(c-f): $p>0.56$ for all analyses). The adjusted analyses for both Models 2 and 3 included the covariates age, degreasing chemical exposure, and industrial chemical exposure.

For Models 4 through 6, the unadjusted and adjusted analyses did not reveal a significant association between hepatitis and current dioxin (Tables 13-3(g,h): $p>0.32$ for all analyses). Each of the adjusted analyses for Models 4 through 6 contained the covariates age and industrial chemical exposure.

Jaundice (Unspecified)

In the unadjusted Model 1 analysis, Ranch Hands and Comparisons were not significantly different in the historical occurrence of jaundice (Table 13-4(a): $p=0.123$). However, stratifying the unadjusted analysis by occupation revealed a marginally significant group difference within the enlisted groundcrew stratum (Table 13-4(a): $p=0.099$, Est. RR=0.36, 95% C.I.=[0.12, 1.09]). For the enlisted groundcrew, 2.7 percent of Comparisons had a history of jaundice while only 1.0 percent of the Ranch Hands had a history of jaundice.

Group-by-race was a significant interaction in the adjusted analysis of Model 1 (Table 13-4(b): $p=0.032$). The adjusted analysis also contained degreasing chemical exposure and the occupation-by-age interaction. Appendix Table I-2-1 presents results stratified by race. After removing the group-by-race interaction, the adjusted analysis detected a marginally significant difference between Ranch Hands and Comparisons (Table 13-4(b): $p=0.100$, Adj. RR=0.62, 95% C.I.=[0.35, 1.11]). A lower percentage of Ranch Hands than Comparisons had a history of jaundice (1.8% vs. 3.0%). The relative risk within the enlisted groundcrew stratum remained marginally significant in the adjusted analysis (Table 13-4(b): $p=0.068$, Adj. RR=0.36, 95% C.I.=[0.12, 1.08]).

The unadjusted and adjusted Model 2 analyses did not reveal a significant relationship between jaundice and initial dioxin (Table 13-4(c,d): $p>0.37$ for both analyses). Age was the only significant covariate in the adjusted model.

Table 13-3.
Analysis of Hepatitis (Non-A, Non-B, and Non-C)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Yes**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***944***	***1.7***	***1.03 (0.53,1.98)***	***0.999***
	Comparison	***1,272***	***1.7***		
Officer	Ranch Hand	363	1.1	1.09 (0.29,4.10)	0.999
	Comparison	495	1.0		
Enlisted Flyer	Ranch Hand	162	3.1	2.12 (0.50,9.02)	0.495
	Comparison	203	1.5		
Enlisted Groundcrew	Ranch Hand	419	1.7	0.73 (0.29,1.85)	0.668
	Comparison	574	2.3		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.05 (0.55,2.03)***	***0.878***	IC*DC (p=0.011) AGE*IC (p=0.018)
Officer	1.11 (0.29,4.18)	0.879	
Enlisted Flyer	2.03 (0.48,8.58)	0.334	
Enlisted Groundcrew	0.78 (0.31,1.97)	0.593	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 13-3. (Continued)
Analysis of Hepatitis (Non-A, Non-B, and Non-C)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	172	1.7	1.11 (0.67,1.83)	0.693
Medium	172	1.7		
High	172	1.7		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
516	1.02 (0.59,1.75)	0.944	AGE (p=0.964) DC (p=0.069) IC (p=0.021)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 13-3. (Continued)
Analysis of Hepatitis (Non-A, Non-B, and Non-C)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,055	1.7		
Background RH	370	1.6	0.98 (0.38,2.52)	0.973
Low RH	258	1.9	1.10 (0.40,2.99)	0.856
High RH	258	1.6	0.89 (0.30,2.65)	0.828
Low plus High RH	516	1.7	0.99 (0.44,2.23)	0.985

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,055			AGE (p=0.224) IC (p=0.077) DC (p=0.111)
Background RH	370	1.22 (0.47,3.16)	0.689	
Low RH	258	1.18 (0.43,3.23)	0.753	
High RH	258	0.72 (0.24,2.19)	0.567	
Low plus High RH	516	0.92 (0.41,2.08)	0.848	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin $\leq$ 10 ppt.
Background (Ranch Hand): Current Dioxin $\leq$ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin $\leq$ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 13-3. (Continued)
Analysis of Hepatitis (Non-A, Non-B, and Non-C)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Yes/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	1.7 (293)	1.7 (296)	1.7 (297)	1.00 (0.71,1.42)	0.991
5	1.7 (297)	1.7 (294)	1.7 (295)	0.92 (0.69,1.25)	0.608
6[c]	1.7 (296)	1.7 (294)	1.7 (295)	1.00 (0.72,1.39)	0.988

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	886	0.91 (0.64,1.30)	0.602	AGE (p=0.740) IC (p=0.002)
5	886	0.86 (0.65,1.15)	0.321	AGE (p=0.713) IC (p=0.002)
6[d]	885	0.93 (0.67,1.27)	0.638	AGE (p=0.857) IC (p=0.002)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 13-4.
Analysis of Jaundice

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Yes**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	*Ranch Hand*	*928*	*1.8*	*0.61 (0.34,1.09)*	*0.123*
	Comparison	*1,248*	*3.0*		
Officer	Ranch Hand	355	2.5	0.61 (0.27,1.35)	0.294
	Comparison	486	4.1		
Enlisted Flyer	Ranch Hand	160	2.5	2.49 (0.45,13.76)	0.506
	Comparison	196	1.0		
Enlisted Groundcrew	Ranch Hand	413	1.0	0.36 (0.12,1.09)	0.099
	Comparison	566	2.7		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	*0.62 (0.35,1.11)***	*0.100***	GROUP*RACE (p=0.032) DC (p<0.093) OCC*AGE (p=0.025)
Officer	0.64 (0.29,1.42)**	0.269**	
Enlisted Flyer	2.34 (0.41,13.39)**	0.341**	
Enlisted Groundcrew	0.36 (0.12,1.08)**	0.068**	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

** Group-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-1 for further analysis of this interaction.

Table 13-4. (Continued)
Analysis of Jaundice

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	168	0.6	1.15 (0.52,2.53)	0.739
Medium	171	0.6		
High	168	0.6		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
	Analysis Results for Log_2 (Initial Dioxin)[c]		
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
507	1.47 (0.66,3.31)	0.372	AGE (p=0.033)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 13-4. (Continued)
Analysis of Jaundice

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	**n**	**Percent Yes**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,035	2.8		
Background RH	363	3.6	1.36 (0.69,2.67)	0.376
Low RH	253	0.4	0.14 (0.02,1.01)	0.052
High RH	254	0.8	0.26 (0.06,1.09)	0.066
Low plus High RH	507	0.6	0.20 (0.06,0.66)	0.008

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	**n**	**Adj. Relative Risk (95% C.I.)[ac]**	**p-Value**	**Covariate Remarks**
Comparison	1,035			DC (p=0.051) OCC*AGE (p=0.015)
Background RH	363	1.28 (0.63,2.57)	0.496	
Low RH	253	0.13 (0.02,0.97)	0.046	
High RH	254	0.30 (0.07,1.31)	0.109	
Low plus High RH	507	0.21 (0.06,0.70)	0.011	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 13-4. (Continued)
Analysis of Jaundice

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Yes/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	3.5 (287)	1.4 (290)	0.7 (293)	0.50 (0.34,0.74)	<0.001
5	3.1 (294)	1.8 (285)	0.7 (291)	0.62 (0.49,0.79)	<0.001
6[c]	3.1 (293)	1.8 (285)	0.7 (291)	0.59 (0.46,0.77)	<0.001

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	870	0.48 (0.32,0.74)	<0.001	AGE (p=0.058) DC (p=0.117) IC (p=0.133)
5	870	0.61 (0.47,0.79)	<0.001	AGE (p=0.053) DC (p=0.128) IC (p=0.121)
6[d]	869	0.59 (0.44,0.77)	<0.001	AGE (p=0.056) DC (p=0.120) IC (p=0.140)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

The unadjusted categorized dioxin analysis (Model 3) revealed a significant difference in the history of jaundice between low plus high Ranch Hands and the Comparison group (Table 13-4(e): p=0.008, Est. RR=0.20, 95% C.I.=[0.06, 0.66]). The unadjusted relative risks were marginally significant for low Ranch Hand and high Ranch Hand categories (Table 13-4(e): p=0.052, Est. RR=0.14, 95% C.I.=[0.02, 1.01], p=0.066, Est. RR=0.26, 95% C.I.=[0.06, 1.09] respectively). The percentages of participants who experienced jaundice in the Comparison, low Ranch Hand, high Ranch Hand, and low plus high Ranch Hand categories were 2.8, 0.4, 0.8, and 0.6 percent respectively.

After adjusting for degreasing chemical exposure and the occupation-by-age interaction, the relative risk for the low plus high Ranch Hand category remained significant (Table 13-4(f): p=0.011, Adj. RR=0.21, 95% C.I.=[0.06, 0.70]). After these same adjustments, the relative risk for the low Ranch Hand category became significant (Table 13-4(f): p=0.046, Adj. RR=0.13, 95% C.I.=[0.02, 0.97]) and the relative risk for the high Ranch Hand category became nonsignificant (Table 13-4(f): p=0.109).

After removing occupation from the adjusted model, the relative risk for the high Ranch Hand category became marginally significant (Appendix Table I-3-1: p=0.078, Adj. RR=0.27, 95% C.I.=[0.06, 1.16]).

As shown in Table 13-4(g), each of the unadjusted analyses for Models 4 through 6 displayed a highly significant inverse association between jaundice and current dioxin (p<0.001, Est. RR=0.50, 95% C.I=[0.34, 0.74], p<0.001; Est. RR=0.62, 95% C.I.=[0.49, 0.79]; and p<0.001, Est. RR=0.59, 95% C.I.=[0.46, 0.77] for Models 4, 5, and 6 respectively).

Each of the adjusted analyses for Models 4 through 6 included age, degreasing chemical exposure, and industrial chemical exposure. Similar to the unadjusted analyses, the adjusted analyses for Models 4 through 6 detected a significant inverse relationship between jaundice and current dioxin (Table 13-4(h): p<0.001, Adj. RR=0.48, 95% C.I.=[0.32, 0.74]; p<0.001, Adj. RR=0.61, 95% C.I.=[0.47, 0.79]; and p<0.001, Adj. RR=0.59, 95% C.I.=[0.44, 0.77] respectively).

Acute and Subacute Necrosis of the Liver

Due to sparse data (one Comparison and no Ranch Hands), analyses were not conducted on acute and subacute necrosis of the liver. Table 13-5 displays sample sizes and frequencies for each model.

Alcoholic Chronic Liver Disease and Cirrhosis

The unadjusted and adjusted Model 1 analyses did not find a significant group difference in the analysis of alcoholic chronic liver disease and cirrhosis (Table 13-6(a,b): p>0.20 for all contrasts). The adjusted analysis contained the covariates age and race, and the occupation-by-lifetime alcohol history interaction.

Table 13-5.
Acute and Subacute Necrosis of the Liver

a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	n	Percent Yes
All	***Ranch Hand***	***952***	***0.0***
	Comparison	***1,280***	***0.1***
Officer	Ranch Hand	367	0.0
	Comparison	501	0.2
Enlisted Flyer	Ranch Hand	162	0.0
	Comparison	203	0.0
Enlisted Groundcrew	Ranch Hand	423	0.0
	Comparison	576	0.0

b) MODEL 2: RANCH HANDS — INITIAL DIOXIN

Initial Dioxin Category Summary Statistics

Initial Dioxin	n	Percent Yes
Low	174	0.0
Medium	173	0.0
High	173	0.0

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 13-5. (Continued)
Acute and Subacute Necrosis of the Liver

c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY		
Dioxin Category	n	Percent Yes
Comparison	1,062	0.0
Background RH	374	0.0
Low RH	260	0.0
High RH	260	0.0
Low plus High RH	520	0.0

d) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN			
	Current Dioxin Category Percent Yes/(n)		
Model[a]	Low	Medium	High
4	0.0 (295)	0.0 (300)	0.0 (299)
5	0.0 (300)	0.0 (297)	0.0 (297)
6	0.0 (299)	0.0 (297)	0.0 (297)

[a] Model 4: Log_2 lipid-adjusted (current dioxin + 1).
Model 5: Log_2 whole-weight (current dioxin + 1).
Model 6: Log_2 whole-weight (current dioxin + 1), adjusted for log_2 total lipids.

Note: RH = Ranch Hands.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Model 4 - Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6 - Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 13-6.
Analysis of Alcoholic Chronic Liver Disease and Cirrhosis

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Percent Yes	Est. Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*888*	*5.4*	*1.00 (0.68,1.47)*	*0.999*
	Comparison	*1,206*	*5.4*		
Officer	Ranch Hand	353	5.7	1.53 (0.80,2.93)	0.265
	Comparison	476	3.8		
Enlisted Flyer	Ranch Hand	147	6.1	0.97 (0.40,2.37)	0.999
	Comparison	191	6.3		
Enlisted Groundcrew	Ranch Hand	388	4.9	0.74 (0.42,1.32)	0.378
	Comparison	539	6.5		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	*0.93 (0.62,1.40)*	*0.733*	RACE (p=0.103) AGE (p=0.373) OCC*DRKYR (p=0.002)
Officer	1.46 (0.73,2.92)	0.283	
Enlisted Flyer	0.92 (0.36,2.40)	0.871	
Enlisted Groundcrew	0.68 (0.37,1.23)	0.202	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 13-6. (Continued)
Analysis of Alcoholic Chronic Liver Disease and Cirrhosis

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	164	6.1	1.05 (0.79,1.39)	0.759
Medium	160	5.0		
High	156	6.4		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED

Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
467	1.02 (0.74,1.39)**	0.915**	INIT*RACE (p=0.004) AGE (p=0.228) DRKYR (p<0.001)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interaction ($p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-2 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.
INIT = Log_2 (initial dioxin).

Table 13-6. (Continued)
Analysis of Alcholic Chronic Liver Disease and Cirrhosis

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Percent Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,005	6.0		
Background RH	354	5.4	0.94 (0.55,1.61)	0.821
Low RH	245	5.7	0.91 (0.50,1.67)	0.767
High RH	235	6.0	0.96 (0.52,1.75)	0.887
Low plus High RH	480	5.8	0.93 (0.59,1.49)	0.776

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	987			DXCAT*RACE (p=0.028) OCC*DRKYR (p=0.002) AGE*DRKYR (p=0.026)
Background RH	347	0.98 (0.54,1.77)**	0.951**	
Low RH	239	0.86 (0.45,1.64)**	0.649**	
High RH	228	0.84 (0.43,1.61)**	0.593**	
Low plus High RH	467	0.85 (0.52,1.39)**	0.517**	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-2 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.
DXCAT = Categorized Dioxin.

Table 13-6. (Continued)
Analysis of Alcoholic Chronic Liver Disease and Cirrhosis

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Yes/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	5.4 (278)	6.0 (282)	5.5 (274)	1.05 (0.86,1.28)	0.655
5	5.3 (282)	5.7 (283)	5.9 (269)	1.04 (0.88,1.24)	0.633
6[c]	5.3 (281)	5.7 (283)	5.9 (269)	1.01 (0.84,1.22)	0.905

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	814	1.03 (0.83,1.27)	0.782	AGE (p=0.279) DRKYR (p<0.001)
5	814	1.03 (0.86,1.23)	0.745	AGE (p=0.276) DRKYR (p<0.001)
6[d]	813	1.00 (0.83,1.21)	0.986	AGE (p=0.298) DRKYR (p<0.001)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Examination of the unadjusted Model 2 results did not reveal a significant association between initial dioxin and alcoholic chronic liver disease and cirrhosis (Table 13-6(c): $p=0.759$).

The adjusted analysis of Model 2 had a significant initial dioxin-by-race interaction (Table 13-6(d): $p=0.004$). Appendix Table I-2-2 presents results stratified by each level of race. The final model also contained age and lifetime alcohol history. After removing the initial dioxin-by-race interaction from the adjusted model, initial dioxin was not significantly associated with alcoholic chronic liver disease and cirrhosis (Table 13-6(d): $p=0.915$).

As shown in Table 13-6(e), the unadjusted Model 3 analysis did not find a significant contrast between any of the Ranch Hand categories and the Comparison group ($p>0.76$ for all contrasts).

Categorized dioxin-by-race was a significant interaction in the adjusted Model 3 analysis (Table 13-6(f): $p=0.028$). Appendix Table I-2-2 shows adjusted results stratified by each level of race. The final model also included two covariate-by-covariate interactions: occupation-by-lifetime alcohol history and age-by-lifetime alcohol history. Without the categorized dioxin-by-race interaction, the adjusted analysis of Model 3 did not detect a significant association between categorized dioxin and alcoholic chronic liver disease (Table 13-6(f): $p>0.51$ for all contrasts).

The unadjusted and adjusted analyses of Models 4 through 6 did not reveal a significant association between current dioxin and alcoholic chronic liver disease and cirrhosis (Table 13-6(g,h): $p>0.63$ for all analyses). Each of the adjusted analyses for Models 4 through 6 contained the covariates age and lifetime alcohol history.

Nonalcoholic Chronic Liver Disease and Cirrhosis

Displayed in Table 13-7(a,b), the unadjusted and adjusted results for Model 1 did not find a significant group difference in the analysis of nonalcoholic chronic liver disease and cirrhosis ($p>0.24$ for all contrasts). The adjusted analysis for Model 1 contained the covariate age.

Similarly, the analyses of Models 2 and 3 did not reveal nonalcoholic chronic liver disease and cirrhosis to be significantly associated with either initial dioxin or categorized dioxin (Table 13-7(c-f): $p>0.61$ for all analyses). For Models 2 and 3, the adjusted analyses contained the covariate age.

The unadjusted and adjusted current dioxin analyses (Models 4 through 6) did not find a significant association between current dioxin and nonalcoholic chronic liver disease and cirrhosis (Table 13-7(g,h): $p>0.38$ for all analyses). Each of the adjusted analyses for Models 4 through 6 contained the covariate age.

Table 13-7.
Analysis of Nonalcoholic Chronic Liver Disease and Cirrhosis

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Yes**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	*Ranch Hand*	*952*	*1.4*	*1.35 (0.62,2.92)*	*0.574*
	Comparison	*1,280*	*1.0*		
Officer	Ranch Hand	367	1.4	2.29 (0.54,9.66)	0.422
	Comparison	501	0.6		
Enlisted Flyer	Ranch Hand	162	1.2	1.26 (0.18,9.02)	0.999
	Comparison	203	1.0		
Enlisted Groundcrew	Ranch Hand	423	1.4	1.02 (0.35,2.97)	0.999
	Comparison	576	1.4		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	*1.36 (0.63,2.96)*	*0.434*	AGE (p=0.095)
Officer	2.34 (0.56,9.88)	0.246	
Enlisted Flyer	1.27 (0.18,9.26)	0.810	
Enlisted Groundcrew	1.02 (0.35,2.96)	0.973	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 13-7. (Continued)
Analysis of Nonalcoholic Chronic Liver Disease and Cirrhosis

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	174	1.1	0.98 (0.55,1.72)	0.932
Medium	173	1.7		
High	173	1.2		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
520	0.87 (0.47,1.59)	0.640	AGE (p=0.246)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 13-7. (Continued)
Analysis of Nonalcoholic Chronic Liver Disease and Cirrhosis

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,062	1.1		
Background RH	374	1.1	1.15 (0.36,3.63)	0.814
Low RH	260	1.5	1.24 (0.38,3.99)	0.721
High RH	260	1.2	0.79 (0.22,2.92)	0.730
Low plus High RH	520	1.3	1.00 (0.38,2.62)	0.999

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,062			AGE (p=0.167)
Background RH	374	1.26 (0.39,4.03)	0.698	
Low RH	260	1.37 (0.42,4.41)	0.602	
High RH	260	0.71 (0.19,2.64)	0.612	
Low plus High RH	520	0.99 (0.38,2.59)	0.980	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 13-7. (Continued)
Analysis of Nonalcoholic Chronic Liver Disease and Cirrhosis

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Yes/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	1.0 (295)	1.0 (300)	1.7 (299)	1.15 (0.78,1.70)	0.480
5	1.0 (300)	1.0 (297)	1.7 (297)	1.17 (0.82,1.65)	0.388
6[c]	1.0 (299)	1.0 (297)	1.7 (297)	1.13 (0.78,1.64)	0.530

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	894	1.10 (0.74,1.63)	0.651	AGE (p=0.340)
5	894	1.12 (0.79,1.59)	0.525	AGE (p=0.352)
6[d]	893	1.07 (0.73,1.57)	0.722	AGE (p=0.316)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Liver Abscess and Sequelae of Chronic Liver Disease

Due to sparse data (one Ranch Hand and one Comparison), analyses were not conducted on liver abscess and sequelae of chronic liver disease. Table 13-8 presents sample sizes and frequencies for each model.

Other Liver Disorders

The category of other liver disorders includes primarily nonspecific elevations of laboratory tests measured at previous AFHS examinations. Only four participants had a medical history of an actual diagnosed disease. The unadjusted and adjusted Model 1 analyses for other liver disorders did not show Ranch Hands and Comparisons to be significantly different (Table 13-9(a,b): $p>0.24$ for all contrasts). The adjusted analysis contained the covariates age, race, and lifetime alcohol history.

As presented in Table 13-9(c), the unadjusted Model 2 results did not reveal a significant association between initial dioxin and other liver disorders ($p=0.177$).

The initial dioxin-by-occupation interaction was significant in the adjusted analysis of Model 2 (Table 13-9(d): $p=0.018$). Appendix Table I-2-3 presents results stratified by occupation. In addition to this interaction, age and race also were significant in the adjusted analysis. When the initial dioxin-by-occupation interaction was removed from the final model, the adjusted Model 2 analysis revealed a significant positive association between other liver disorders and initial dioxin (Table 13-9(d): $p=0.046$, Adj. RR=1.18, 95% C.I.=[1.00, 1.40]).

With occupation removed, the adjusted Model 2 results matched the unadjusted results. The association between other liver disorders and initial dioxin was nonsignificant (Appendix Table I-3-3(a): $p=0.203$).

The unadjusted Model 3 analysis found a marginally significant difference in the history of other liver disorders between the high Ranch Hands and the Comparison group (Table 13-9(e): $p=0.081$, Est. RR=1.30, 95% C.I.=[0.97, 1.74]). The percentage of participants with a history of other liver disorders was higher for high Ranch Hands than for the Comparison group (34.2% vs. 27.4%).

The adjusted Model 3 analysis contained a significant categorized dioxin-by-degreasing chemical exposure interaction (Table 13-9(f): $p=0.042$). Appendix Table I-2-3 displays adjusted results stratified by degreasing chemical exposure. In addition to the categorized dioxin-by-degreasing chemical exposure interaction, the occupation-by-race interaction and two covariates, age and lifetime alcohol history, were significant in the adjusted analysis of Model 3. The relative risk for high Ranch Hands became significant when the categorized dioxin-by-degreasing chemical exposure was removed from the adjusted analysis (Table 13-9(f): $p=0.048$, Adj. RR=1.37, 95% C.I.=[1.00, 1.86]).

Table 13-8.
Liver Abscess and Sequelae of Chronic Liver Disease

a) MODEL 1: RANCH HANDS VS. COMPARISONS			
Occupational Category	Group	n	Percent Yes
All	***Ranch Hand***	***952***	***0.1***
	Comparison	***1,281***	***0.1***
Officer	Ranch Hand	367	0.0
	Comparison	502	0.2
Enlisted Flyer	Ranch Hand	162	0.0
	Comparison	203	0.0
Enlisted Groundcrew	Ranch Hand	423	0.2
	Comparison	576	0.0

b) MODEL 2: RANCH HANDS — INITIAL DIOXIN		
Initial Dioxin Category Summary Statistics		
Initial Dioxin	n	Percent Yes
Low	174	0.0
Medium	173	0.0
High	173	0.6

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 13-8. (Continued)
Liver Abscess and Sequelae of Chronic Liver Disease

c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY		
Dioxin Category	**n**	**Percent Yes**
Comparison	1,063	0.1
Background RH	374	0.0
Low RH	260	0.0
High RH	260	0.4
Low plus High RH	520	0.2

d) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN			
	Current Dioxin Category Percent Yes/(n)		
Model[a]	**Low**	**Medium**	**High**
4	0.0 (295)	0.0 (300)	0.3 (299)
5	0.0 (300)	0.0 (297)	0.3 (297)
6	0.0 (299)	0.0 (297)	0.3 (297)

[a] Model 4: Log_2 lipid-adjusted (current dioxin + 1).
Model 5: Log_2 whole-weight (current dioxin + 1).
Model 6: Log_2 whole-weight (current dioxin + 1), adjusted for $\log_2$ total lipids.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Model 4 - Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6 - Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 13-9.
Analysis of Other Liver Disorders

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Yes**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***948***	***30.1***	***1.11 (0.92,1.34)***	***0.281***
	Comparison	***1,270***	***27.9***		
Officer	Ranch Hand	364	29.4	1.12 (0.83,1.51)	0.513
	Comparison	494	27.1		
Enlisted Flyer	Ranch Hand	162	25.3	0.91 (0.57,1.46)	0.791
	Comparison	203	27.1		
Enlisted Groundcrew	Ranch Hand	422	32.5	1.19 (0.91,1.56)	0.240
	Comparison	573	28.8		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.11 (0.92,1.34)***	***0.272***	AGE (p=0.711) RACE (p<0.001) DRKYR (p=0.003)
Officer	1.14 (0.84,1.54)	0.398	
Enlisted Flyer	0.87 (0.54,1.41)	0.579	
Enlisted Groundcrew	1.18 (0.89,1.56)	0.240	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 13-9. (Continued)
Analysis of Other Liver Disorders

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	173	26.6	1.10 (0.96,1.27)	0.177
Medium	173	32.4		
High	173	35.8		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
519	1.18 (1.00,1.40)**	0.046**	INIT*OCC (p=0.018) AGE (p=0.142) RACE (p=0.002)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-3 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 13-9. (Continued)
Analysis of Other Liver Disorders

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	**n**	**Percent Yes**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,053	27.4		
Background RH	371	25.1	0.96 (0.73,1.26)	0.750
Low RH	259	29.0	1.04 (0.77,1.41)	0.787
High RH	260	34.2	1.30 (0.97,1.74)	0.081
Low plus High RH	519	31.6	1.17 (0.93,1.47)	0.193

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	**n**	**Adj. Relative Risk (95% C.I.)[ac]**	**p-Value**	**Covariate Remarks**
Comparison	1,036			DXCAT*DC (p=0.042) AGE (p=0.972) DRKYR (p<0.001) OCC*RACE (p=0.037)
Background RH	365	0.96 (0.72,1.27)**	0.761**	
Low RH	253	1.03 (0.75,1.40)**	0.860**	
High RH	253	1.37 (1.00,1.86)**	0.048**	
Low plus High RH	506	1.18 (0.93,1.50)**	0.169**	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-3 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 13-9. (Continued)
Analysis of Other Liver Disorders

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Yes/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	23.5 (293)	29.9 (298)	33.1 (299)	1.15 (1.04,1.27)	0.007
5	23.9 (297)	29.1 (296)	33.7 (297)	1.14 (1.05,1.24)	0.003
6[c]	24.0 (296)	29.1 (296)	33.7 (297)	1.11 (1.01,1.21)	0.033

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	871	1.19 (1.06,1.34)**	0.004**	CURR*OCC (p=0.004) CURR*DC (p=0.005) AGE (p=0.597) RACE (p=0.030) DRKYR (p=0.023)
5	871	1.18 (1.06,1.31)**	0.001**	CURR*OCC (p=0.007) CURR*DC (p=0.011) AGE (p=0.573) RACE (p=0.028) DRKYR (p=0.025)
6[d]	870	1.14 (1.02,1.27)**	0.018**	CURR*OCC (p=0.011) CURR*DC (p=0.010) AGE (p=0.528) RACE (p=0.022) DRKYR (p=0.028)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interactions ($p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table I-2-3 for further analysis of these interactions.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.
CURR: Log_2 (current dioxin + 1).

Deleting occupation from the final model had produced a small change in the adjusted results. When occupation and the categorized dioxin-by-degreasing chemical interaction were removed from the adjusted model, the relative risk for the high Ranch Hand category became marginally significant (Appendix Table I-3-3: p=0.077).

The unadjusted analyses for Models 4 through 6 revealed a significant positive association between current dioxin and other liver disorders (Table 13-9(g): p=0.007, Est. RR=1.15, 95% C.I.=[1.04, 1.27]; p=0.003, Est. RR=1.14, 95% C.I.=[1.05, 1.24]; and p=0.033, Est. RR=1.11, 95% C.I.=[1.01, 1.21] for Models 4, 5, and 6 respectively).

Each of the adjusted analyses for Models 4 through 6 had a significant current dioxin-by-occupation interaction and a significant current dioxin-by-degreasing chemical interaction (Table 13-9(h): p=0.004 and p=0.005 for Model 4, p=0.007 and p=0.011 for Model 5, and p=0.011 and p=0.010 for Model 6). Age, race and lifetime alcohol history also were included in the adjusted analyses of Models 4 through 6. Appendix Table I-2-3 presents results stratified separately by occupation and degreasing chemical exposure. The adjusted analyses of Models 4 through 6 found a significant positive association between current dioxin and other liver disorders when both the current dioxin-by-occupation and current dioxin-by-degreasing chemical exposure interactions were removed from each of the adjusted models (Table 13-9(h): p=0.004, Adj. RR=1.19, 95% C.I.=[1.06, 1.34]; p=0.001, Adj. RR=1.18, 95% C.I.=[1.06, 1.31]; and p=0.018, Adj. RR=1.14, 95% C.I.=[1.02, 1.27] respectively.

Omitting occupation from the adjusted analysis of Models 4 and 5 had no effect on the results of either of these models. However, deleting occupation from the adjusted analysis of Model 6 affected the significance of the association between current dioxin and other liver disorders. Without occupation and the current dioxin-by-occupation and the current dioxin-by-degreasing chemical interactions, the Model 6 analysis detected a marginally significant positive association instead of a significant association between current dioxin and other liver disorders (Appendix Table I-3-3: p=0.056).

Hepatomegaly

The unadjusted Model 1 results did not reveal a significant group difference in the historical occurrence of hepatomegaly (Table 13-10(a): p=0.163). However, stratifying the unadjusted analysis by occupation revealed a marginally significant group difference within the enlisted groundcrew stratum (Table 13-10(a): p=0.052, Est. RR=0.35, 95% C.I.=[0.13, 0.95]). In this stratum, Ranch Hands were less than half as likely as Comparisons to have a history of hepatomegaly (1.2% vs. 3.3%).

The adjusted Model 1 analysis contained the group-by-occupation interaction (Table 13-10(b): p=0.048) and two covariates, age and lifetime alcohol history. In contrast to the unadjusted analysis, the adjusted analysis detected a marginally significant overall difference when the group-by-occupation interaction was removed from the final model (Table 13-10(b): p=0.098, Adj. RR=0.61, 95% C.I.=[0.33, 1.11]). The group contrast within the enlisted groundcrew stratum became significant when the adjusted analysis was stratified by occupation (Table 13-10(b): p=0.031, Adj. RR=0.33, 95% C.I.=[0.12, 0.90]).

Table 13-10.
Analysis of Hepatomegaly

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Yes**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	*Ranch Hand*	*951*	*1.7*	*0.63 (0.34,1.14)*	*0.163*
	Comparison	*1,279*	*2.7*		
Officer	Ranch Hand	367	1.4	0.56 (0.20,1.61)	0.400
	Comparison	500	2.4		
Enlisted Flyer	Ranch Hand	162	3.7	2.56 (0.63,10.42)	0.306
	Comparison	203	1.5		
Enlisted Groundcrew	Ranch Hand	422	1.2	0.35 (0.13,0.95)	0.052
	Comparison	576	3.3		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	*0.61 (0.33, 1.11)***	*0.098***	GROUP*OCC (p=0.048) AGE (p<0.001) DRKYR (p=0.006)
Officer	0.54 (0.19,1.57)**	0.261**	
Enlisted Flyer	2.61 (0.64,10.66)**	0.182**	
Enlisted Groundcrew	0.33 (0.12,0.90)**	0.031**	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

** Group-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction.

Table 13-10. (Continued)
Analysis of Hepatomegaly

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	174	1.1	1.01 (0.61,1.67)	0.980
Medium	173	2.9		
High	172	1.2		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
506	1.00 (0.55,1.82)	0.991	AGE (p=0.011) OCC (p=0.132) DRKYR (p=0.053)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 13-10. (Continued)
Analysis of Hepatomegaly

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,061	2.6		
Background RH	374	1.3	0.53 (0.20,1.38)	0.192
Low RH	260	0.8	0.27 (0.06,1.13)	0.073
High RH	259	2.7	0.98 (0.42,2.28)	0.960
Low plus High RH	519	1.7	0.61 (0.29,1.32)	0.210

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,043			AGE (p=0.012) DC (p=0.115) DRKYR (p=0.006)
Background RH	367	0.51 (0.19,1.38)	0.186	
Low RH	254	0.26 (0.06,1.09)	0.066	
High RH	252	1.02 (0.43,2.44)	0.958	
Low plus High RH	506	0.61 (0.28,1.32)	0.211	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin $\leq$ 10 ppt.
Background (Ranch Hand): Current Dioxin $\leq$ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin $\leq$ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 13-10. (Continued)
Analysis of Hepatomegaly

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Yes/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	1.0 (295)	1.3 (300)	2.3 (298)	1.00 (0.70,1.44)	0.994
5	1.3 (300)	1.0 (297)	2.4 (296)	0.96 (0.70,1.30)	0.773
6[c]	1.3 (299)	1.0 (297)	2.4 (296)	0.97 (0.69,1.35)	0.850

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	873	0.92 (0.61,1.39)	0.683	AGE (p=0.009) OCC (p=0.038) DRKYR (p=0.080)
5	873	0.88 (0.63,1.23)	0.462	AGE (p=0.009) OCC (p=0.029) DRKYR (p=0.082)
6[d]	872	0.89 (0.61,1.29)	0.534	AGE (p=0.008) OCC (p=0.029) DRKYR (p=0.088)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

The unadjusted and adjusted Model 2 analyses did not reveal significant associations between hepatomegaly and initial dioxin (Table 13-10(c,d): $p>0.98$ for both analyses). The adjusted analysis for Model 2 contained the covariates age, occupation, and lifetime alcohol history.

The unadjusted Model 3 results revealed a marginally significant difference in hepatomegaly between low Ranch Hands and the Comparison group (Table 13-10(e): $p=0.073$, Est. RR=0.27, 95% C.I.=[0.06, 1.13]). Low Ranch Hands were less likely than Comparisons to have a history of hepatomegaly (0.8% vs. 2.6%). After adjusting for age, degreasing chemical exposure, and lifetime alcohol history, the relative risk for low Ranch Hands remained marginally significant (Table 13-10(f): $p=0.066$, Adj. RR=0.26, 95% C.I.=[0.06, 1.09]),

The unadjusted and adjusted analyses of Models 4 through 6 found no significant associations between hepatomegaly and current dioxin (Table 13-10(g,h): $p>0.46$ for all analyses). Each of the adjusted analyses for Models 4 through 6 contained the covariates age, occupation, and lifetime alcohol history.

Physical Examination Variable

Current Hepatomegaly

The unadjusted and adjusted Model 1 analyses of current hepatomegaly did not reveal significant differences between Ranch Hands and Comparisons (Table 13-11(a,b): $p>0.63$ for all contrasts). Lifetime alcohol history was the only significant covariate in the adjusted analysis.

The unadjusted Model 2 analysis did not reveal a significant association between current hepatomegaly and initial dioxin (Table 13-11(c): $p=0.632$). The unadjusted and adjusted Model 2 results were identical because no covariates were retained in the final model.

The unadjusted and adjusted Model 3 results did not show any of the Ranch Hand categories to be significantly different from the Comparison group (Table 13-11(e,f): $p\geq0.31$ for all contrasts). Lifetime alcohol history was the only significant covariate in the adjusted analysis.

For Models 4 through 6, the unadjusted and adjusted analyses did not show a significant association between current hepatomegaly and current dioxin (Table 13-11(g,h): $p>0.38$ for all analyses). Each of the adjusted analyses included lifetime alcohol history.

Table 13-11.
Analysis of Current Hepatomegaly

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	Group	n	Percent Yes	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***942***	***0.6***	***0.80 (0.29,2.20)***	***0.854***
	Comparison	***1,254***	***0.8***		
Officer	Ranch Hand	364	0.5	0.68 (0.12,3.72)	0.972
	Comparison	495	0.8		
Enlisted Flyer	Ranch Hand	162	0.6	--	--
	Comparison	198	0.0		
Enlisted Groundcrew	Ranch Hand	416	0.7	0.67 (0.17,2.70)	0.822
	Comparison	561	1.1		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	***0.87 (0.31,2.46)***	***0.785***	DRKYR (p=0.024)
Officer	0.66 (0.12,3.63)	0.633	
Enlisted Flyer	--	--	
Enlisted Groundcrew	0.79 (0.19,3.35)	0.747	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

--: Relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities.

Table 13-11. (Continued)
Analysis of Current Hepatomegaly

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	173	0.6	0.83 (0.38,1.81)	0.632
Medium	171	1.2		
High	172	0.6		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[a]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
516	0.83 (0.38,1.81)	0.632	

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 13-11. (Continued)
Analysis of Current Hepatomegaly

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Percent Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,043	0.9		
Background RH	371	0.3	0.34 (0.04,2.72)	0.310
Low RH	258	0.4	0.43 (0.05,3.42)	0.425
High RH	258	1.2	1.25 (0.33,4.71)	0.738
Low plus High RH	516	0.8	0.85 (0.26,2.78)	0.783

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,025			DRKYR (p=0.030)
Background RH	364	0.41 (0.05,3.34)	0.405	
Low RH	252	0.51 (0.06,4.17)	0.532	
High RH	251	1.27 (0.32,4.97)	0.735	
Low plus High RH	503	0.92 (0.27,3.11)	0.890	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 13-11. (Continued)
Analysis of Current Hepatomegaly

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Yes/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	0.0 (292)	0.7 (299)	1.0 (296)	1.25 (0.72,2.20)	0.440
5	0.3 (296)	0.3 (297)	1.0 (294)	1.26 (0.76,2.09)	0.380
6[c]	0.3 (295)	0.3 (297)	1.0 (294)	1.23 (0.72,2.12)	0.457

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	867	1.21 (0.71,2.09)	0.495	DRKYR (p=0.092)
5	867	1.21 (0.75,1.97)	0.438	DRKYR (p=0.095)
6[d]	866	1.19 (0.70,2.03)	0.517	DRKYR (p=0.095)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Laboratory Examination Variables

AST (Continuous)

The unadjusted Model 1 analysis revealed a marginally significant difference in the mean level of AST between Ranch Hands and Comparisons (Table 13-12(a): p=0.082). Ranch Hands had a lower mean level of AST than Comparisons (23.11 U/L vs. 23.76 U/L). Stratifying the unadjusted results by occupation revealed a significant difference in the mean levels of AST within the enlisted flyer stratum (Table 13-12(a): p=0.022), with a higher mean level of AST in the Comparisons than in the Ranch Hands (23.17 U/L vs. 21.28 U/L).

The adjusted Model 1 analysis included occupation and two covariate-by-covariate interactions: lifetime alcohol history-by-degreasing chemical exposure and current alcohol use-by-industrial chemical exposure. In contrast to the unadjusted analysis, the adjusted analysis of AST did not show a significant difference between the Ranch Hands and Comparisons (Table 13-12(b): p=0.138). When the adjusted analysis was stratified by occupation, the group contrast within the enlisted flyer stratum became marginally significant (Table 13-12(b): p=0.071).

The unadjusted Model 2 results did not reveal a significant association between AST and initial dioxin (Table 13-12(c): p=0.362). The interaction between initial dioxin and current alcohol use was significant in the adjusted analysis of Model 2 (Table 13-12(d): p=0.005). Appendix Table I-2-4 displays adjusted results stratified by current alcohol use. These results reveal a synergism between current alcohol consumption and initial dioxin exposure. The relationship between AST and TCDD (i.e., slope coefficient) increased for higher alcohol consumption levels. Besides the initial dioxin-by-current alcohol use interaction, the adjusted model contained the covariates occupation and degreasing chemical exposure, and the current alcohol use-by-industrial chemical exposure interaction. AST was not significantly associated with initial dioxin when the initial dioxin-by-current alcohol use interaction was removed from the adjusted model (Table 13-12(d): p=0.433).

The unadjusted and adjusted Model 3 analyses did not show any of the Ranch Hand categories to be significantly different from the Comparison group (Table 13-12(e,f): p>0.19 for all contrasts). The adjusted analysis included occupation and two covariate-by-covariate interactions: lifetime alcohol history-by-degreasing chemical exposure and current alcohol use-by-industrial chemical exposure.

The unadjusted analyses of Models 4 and 6 did not find a significant association between AST and current dioxin (Table 13-12(g): p=0.166 and p=0.253 for Models 4 and 6 respectively). However, the unadjusted Model 5 analysis uncovered a marginally significant positive association between AST and current dioxin (Table 13-12(g): p=0.095, Est. Slope= 0.0120).

Each of the adjusted analyses for Models 4 through 6 contained a significant current dioxin-by-current alcohol use interaction (Table 13-12(h): p=0.003 for each model). Appendix Table I-2-4 presents adjusted results stratified by current alcohol use for each of the models. In addition to the current dioxin-by-current alcohol use interaction, each of the

Table 13-12.
Analysis of AST (U/L)
(Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***939***	***23.11***	***-0.66 --***	***0.082***
	Comparison	***1,253***	***23.76***		
Officer	Ranch Hand	361	23.67	-0.70 --	0.258
	Comparison	495	24.37		
Enlisted Flyer	Ranch Hand	162	21.28	-1.89 --	0.022
	Comparison	196	23.17		
Enlisted Groundcrew	Ranch Hand	416	23.37	-0.08 --	0.887
	Comparison	562	23.45		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED						
Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]	Covariate Remarks[d]
All	***Ranch Hand***	***917***	***22.87***	***-0.55 --***	***0.138***	OCC (p=0.010)
	Comparison	***1,232***	***23.41***			DRKYR*DC (p=0.010)
Officer	Ranch Hand	357	23.55	-0.61 --	0.319	ALC*IC (p=0.002)
	Comparison	487	24.15			
Enlisted Flyer	Ranch Hand	156	21.33	-1.57 --	0.071	
	Comparison	195	22.90			
Enlisted Groundcrew	Ranch Hand	404	23.41	-0.11 --	0.851	
	Comparison	550	23.51			

[a] Transformed from natural logarithm scale.

[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

[c] P-values based on difference of means on natural logarithm scale.

[d] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 13-12. (Continued)
Analysis of AST (U/L)
(Continuous)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				**Analysis Results for Log_2 (Initial Dioxin)[b]**		
Initial Dioxin	**n**	**Mean[a]**	**Adj. Mean[ab]**	**R^2**	**Slope (Std. Error)[c]**	**p-Value**
Low	173	22.42	22.49	0.009	0.0113 (0.0124)	0.362
Medium	170	23.53	23.57			
High	172	23.65	23.54			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)[d]**			
Initial Dioxin	**n**	**Adj. Mean[ad]**	**R^2**	**Adj. Slope (Std. Error)[c]**	**p-Value**	**Covariate Remarks**
Low	171	22.01**	0.094	0.0110 (0.0140)**	0.433**	INIT*ALC (p=0.005) OCC (p=0.017) DC (p=0.144) ALC*IC (p=0.003)
Medium	167	23.03**				
High	170	22.88**				

[a] Transformed from the natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Slope and standard error based on natural logarithm of AST versus $\log_2$ (initial dioxin).

[d] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interaction ($p \leq 0.05$); adjusted mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-4 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 13-12. (Continued)
Analysis of AST (U/L)
(Continuous)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,043	23.66	23.65		
Background RH	369	22.93	23.15	-0.50 --	0.340
Low RH	257	23.22	23.14	-0.51 --	0.394
High RH	258	23.17	22.96	-0.69 --	0.248
Low plus High RH	515	23.19	23.05	-0.60 --	0.195

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Mean[ae]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]	Covariate Remarks
Comparison	1,025	23.20			OCC (p=0.007) DRKYR*DC (p=0.013) ALC*IC (p<0.001)
Background RH	362	22.73	-0.47 --	0.370	
Low RH	251	22.91	-0.29 --	0.616	
High RH	251	22.79	-0.41 --	0.496	
Low plus High RH	502	22.85	-0.35 --	0.442	

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not presented because analysis was performed on natural logarithm scale.

[d] P-value is based on difference of means on natural logarithm scale.

[e] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 13-12. (Continued)
Analysis of AST (U/L)
(Continuous)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED						
	Current Dioxin Category Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)		
Model[b]	Low	Medium	High	R^2	Slope (Std. Error)[c]	p-Value
4	22.59 (290)	23.62 (298)	23.04 (296)	0.002	0.0116 (0.0084)	0.166
5	22.57 (294)	23.27 (297)	23.41 (293)	0.003	0.0120 (0.0072)	0.095
6[d]	22.74 (293)	23.28 (297)	23.22 (293)	0.005	0.0088 (0.0077)	0.253

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED							
	Current Dioxin Category Adjusted Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)			
Model[b]	Low	Medium	High	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
4	21.88** (287)	23.19** (290)	22.46** (287)	0.080	0.0137 (0.0094)**	0.147**	CURR*ALC (p=0.003) OCC (p=0.004) AGE*DRKYR (p=0.046) ALC*IC (p<0.001) DRKYR*DC (p=0.011)
5	21.77** (290)	22.80** (290)	22.95** (284)	0.081	0.0135 (0.0080)**	0.090**	CURR*ALC (p=0.003) OCC (p=0.003) AGE*DRKYR (p=0.046) ALC*IC (p<0.001) DRKYR*DC (p=0.012)
6[e]	21.89** (289)	22.82** (290)	22.80** (284)	0.083	0.0115 (0.0086)**	0.184**	CURR*ALC (p=0.003) OCC (p=0.003) AGE*DRKYR (p=0.038) ALC*IC (p<0.001) DRKYR*DC (p=0.011)

[a] Transformed from natural logarithm scale.

[b] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for $\log_2$ total lipids.

[c] Slope and standard error based on natural logarithm of AST versus $\log_2$ (current dioxin + 1).

[d] Adjusted for $\log_2$ total lipids.

[e] Adjusted for $\log_2$ total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($p \leq 0.05$); adjusted mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-4 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

adjusted analyses for Models 4 through 6 contained the covariate occupation and three covariate-by-covariate interactions: age-by-lifetime alcohol history, current alcohol use-by-industrial chemical exposure, and lifetime alcohol history-by-degreasing chemical exposure. For the Model 4 analysis, current dioxin was not significantly associated with AST when the current dioxin-by-current alcohol use interaction was removed from the adjusted model (Table 13-12(h): p=0.147). The adjusted analysis of Model 5 was similar to its unadjusted analysis after the current dioxin-by-current alcohol use interaction was removed from the final model. Current dioxin was marginally associated with AST (Table 13-12(h): p=0.090, Adj. Slope=0.0135). The adjusted Model 6 analysis did not reveal a significant association between current dioxin and AST when the current dioxin-by-current alcohol use interaction was removed from the final model (Table 13-12(h): p=0.184).

AST (Discrete)

For Model 1, the unadjusted analysis did not reveal a significant group difference in the percent of participants with high levels of AST (Table 13-13(a): p>0.31 for all contrasts). The interaction between group and current alcohol use was significant in the adjusted analysis of Model 1 (Table 13-13(b): p=0.017). Appendix Table I-2-5 presents adjusted results stratified by current alcohol use. Race, degreasing chemical exposure, industrial chemical exposure, and lifetime alcohol history also were significant in the adjusted analysis. The adjusted analysis did not reveal any significant group contrast when the group-by-current alcohol use interaction was removed from the final model (Table 13-13(b): p>0.25 for all contrasts).

Shown in Table 13-13(c), the unadjusted Model 2 results did not disclose a significant association between AST and initial dioxin (p=0.895). The adjusted Model 2 analysis contained lifetime alcohol history and a significant interaction between initial dioxin and current alcohol use (Table 13-13(d): p=0.025). Results stratified by current alcohol use are presented in Appendix Table I-2-5. After removing the interaction between initial dioxin and current alcohol use from the final model, the adjusted analysis did not reveal a significant association between AST and initial dioxin (Table 13-13(d): p=0.679).

The unadjusted Model 3 analysis did not find a significant difference in the percentage of participants with high AST levels between any of the Ranch Hand categories and the Comparison group (Table 13-13(e): p>0.19 for all contrasts).

The interaction between categorized dioxin and current alcohol use was significant in the adjusted Model 3 analysis (Table 13-13(f): p=0.015). Appendix Table I-2-5 presents adjusted results stratified by current alcohol use. The final model also contained industrial chemical exposure, degreasing chemical exposure, and lifetime alcohol history. The adjusted analysis did not reveal a significant association between AST and categorized dioxin for each contrast when the categorized dioxin-by-current alcohol use interaction was removed from the adjusted model (Table 13-13(f): p>0.20).

None of the unadjusted analyses for Models 4 through 6 revealed a significant association between AST and current dioxin (Table 13-13(g): p>0.23 for each analysis). For Models 4 through 6, all of the adjusted analyses contained a significant interaction

Table 13-13.
Analysis of AST
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent High**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	*Ranch Hand*	*939*	*2.7*	*0.75 (0.46,1.24)*	*0.316*
	Comparison	*1,253*	*3.5*		
Officer	Ranch Hand	361	3.6	0.89 (0.44,1.81)	0.881
	Comparison	495	4.0		
Enlisted Flyer	Ranch Hand	162	1.2	0.34 (0.07,1.65)	0.286
	Comparison	196	3.6		
Enlisted Groundcrew	Ranch Hand	416	2.4	0.79 (0.36,1.74)	0.698
	Comparison	562	3.0		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	*0.85 (0.51,1.41)***	*0.519***	GROUP*ALC (p=0.017)
Officer	0.94 (0.45,1.96)**	0.875**	RACE (p=0.137)
Enlisted Flyer	0.39 (0.08,1.95)**	0.253**	DC (p=0.091)
Enlisted Groundcrew	0.93 (0.41,2.13)**	0.869**	IC (p=0.035)
			DRKYR (p=0.044)

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

** Group-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-5 for further analysis of this interaction.

Table 13-13. (Continued)
Analysis of AST
(Discrete)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	173	2.3	1.03 (0.69,1.52)	0.895
Medium	170	2.9		
High	172	2.9		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
502	0.92 (0.60,1.40)**	0.679**	INIT*ALC (p=0.025) DRKYR (p=0.080)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-5 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 13-13. (Continued)
Analysis of AST
(Discrete)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	**n**	**Percent High**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,043	3.2		
Background RH	369	2.2	0.78 (0.35,1.71)	0.529
Low RH	257	3.5	1.06 (0.50,2.25)	0.885
High RH	258	1.9	0.53 (0.20,1.38)	0.192
Low plus High RH	515	2.7	0.78 (0.41,1.48)	0.449

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	**n**	**Adj. Relative Risk (95% C.I.)[ac]**	**p-Value**	**Covariate Remarks**
Comparison	1,025			DXCAT*ALC (p=0.015) IC (p=0.008) DC (p=0.020) DRKYR (p=0.141)
Background RH	362	0.91 (0.41,2.05)**	0.824**	
Low RH	251	1.24 (0.57,2.71)**	0.587**	
High RH	251	0.52 (0.19,1.42)**	0.201**	
Low plus High RH	502	0.85 (0.43,1.65)**	0.628**	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-5 for further analysis of this interaction.

Note: Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 13-13. (Continued)
Analysis of AST
(Discrete)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent High/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	1.4 (290)	4.4 (298)	1.7 (296)	1.13 (0.86,1.50)	0.393
5	1.4 (294)	3.4 (297)	2.7 (293)	1.16 (0.91,1.49)	0.237
6[c]	1.4 (293)	3.4 (297)	2.7 (293)	1.08 (0.83,1.41)	0.578

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	864	1.19 (0.82,1.71)**	0.352**	CURR*ALC (p=0.012) OCC (p=0.029) IC (p=0.088) DC (p=0.003) DRKYR (p=0.087)
5	864	1.22 (0.88,1.69)**	0.231**	CURR*ALC (p=0.018) OCC (p=0.018) IC (p=0.103) DC (p=0.003) DRKYR (p=0.088)
6[d]	863	1.14 (0.81,1.61)**	0.451**	CURR*ALC (p=0.016) OCC (p=0.018) IC (p=0.112) DC (p=0.004) DRKYR (p=0.086)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-5 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

between current dioxin and current alcohol use (Table 13-13(h): p=0.012, p=0.018, and p=0.016 for Models 4, 5, and 6 respectively). Similar to the Model 2 findings for initial dioxin, the interaction results displayed in Table I-2-4 reveal a synergism between current alcohol consumption and current dioxin levels, with the association between current dioxin levels and AST becoming stronger for higher alcohol consumption levels. In addition to the current dioxin-by-current alcohol use interaction, each of the adjusted analyses contained the covariates occupation, industrial chemical exposure, degreasing chemical exposure and lifetime alcohol history. After removing the current dioxin-by-current alcohol use interaction from each of the three adjusted models, AST was not significantly associated with current dioxin in any of the adjusted analyses (Table 13-13(h): p>0.23 for all analyses).

ALT (Continuous)

The unadjusted Model 1 results showed a significant group difference in the mean levels of ALT (Table 13-14(a): p=0.047). The mean level of ALT was lower for Ranch Hands than Comparisons (26.85 U/L vs. 27.92 U/L). Stratification by occupation revealed a significant group difference in the mean levels of ALT within the enlisted flyer stratum (Table 13-14(a): p=0.010). Again, the mean level of ALT was lower for Ranch Hands than Comparisons (24.76 U/L vs. 28.11 U/L).

After adjusting for covariates, the difference in mean levels of ALT between Ranch Hands and Comparisons became marginally significant (Table 13-14(b): p=0.080). A significant difference in mean levels of ALT persisted within the enlisted flyer stratum after the adjusted analysis was stratified by occupation (Table 13-14(b): p=0.026). The adjusted model contained race, lifetime alcohol history, degreasing chemical exposure and the age-by-current alcohol use interaction.

The unadjusted and adjusted Model 2 analyses did not reveal a significant association between ALT and initial dioxin (Tables 13-14(c,d): p>0.11 for both analyses). Age, occupation, current alcohol use, and degreasing chemical exposure were significant covariates in the adjusted analysis.

In Table 13-14(e), the unadjusted Model 3 results revealed a significantly lower mean level of ALT for background Ranch Hands than for the Comparison group (p=0.011, Difference=-1.85). The mean levels of ALT for the Ranch Hands and Comparisons were 25.91 U/L and 27.76 U/L respectively.

After adjusting for lifetime alcohol history, degreasing chemical exposure, and the age-by-current alcohol use interaction, the difference in the mean levels of ALT between the background Ranch Hands and Comparisons became marginally significant (Table 13-14(f): p=0.072, Adj. Difference=-1.31).

The unadjusted results for Models 4, 5, and 6 showed highly significant positive associations between ALT and current dioxin (Table 13-14(g): p<0.001, Est. Slope=0.0476; p<0.001, Est. Slope=0.0429; and p<0.001, Est. Slope=0.0410 respectively).

Table 13-14.
Analysis of ALT (U/L)
(Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	*Ranch Hand*	*939*	*26.85*	*-1.07 --*	*0.047*
	Comparison	*1,253*	*27.92*		
Officer	Ranch Hand	361	26.76	-0.66 --	0.424
	Comparison	495	27.42		
Enlisted Flyer	Ranch Hand	162	24.76	-3.35 --	0.010
	Comparison	196	28.11		
Enlisted Groundcrew	Ranch Hand	416	27.80	-0.52 --	0.544
	Comparison	562	28.32		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]	Covariate Remarks[d]
All	*Ranch Hand*	*917*	*26.12*	*-0.91 --*	*0.080*	RACE (p=0.120)
	Comparison	*1,232*	*27.03*			DRKYR (p=0.040)
Officer	Ranch Hand	357	26.81	-0.40 --	0.633	DC (p=0.146) AGE*ALC (p=0.006)
	Comparison	487	27.22			
Enlisted Flyer	Ranch Hand	156	24.59	-2.79 --	0.026	
	Comparison	195	27.39			
Enlisted Groundcrew	Ranch Hand	404	26.17	-0.63 --	0.423	
	Comparison	550	26.80			

[a] Transformed from natural logarithm scale.

[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

[c] P-values based on difference of means on natural logarithm scale.

[d] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 13-14. (Continued)
Analysis of ALT (U/L)
(Continuous)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	173	26.08	26.33	0.038	0.0244 (0.0154)	0.113
Medium	170	28.59	28.68			
High	172	29.21	28.83			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[d]			
Initial Dioxin	n	Adj. Mean[ad]	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
Low	171	26.27	0.088	0.0171 (0.0175)	0.328	AGE (p=0.001) OCC (p=0.059) ALC (p=0.009) DC (p=0.068)
Medium	167	28.34				
High	170	27.94				

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Slope and standard error based on natural logarithm of ALT versus $\log_2$ (initial dioxin).

[d] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 13-14. (Continued)
Analysis of ALT (U/L)
(Continuous)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED					
Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,043	27.78	27.76		
Background RH	369	25.35	25.91	-1.85 --	0.011
Low RH	257	27.37	27.27	-0.48 --	0.571
High RH	258	28.47	27.82	0.06 --	0.944
Low plus High RH	515	27.92	27.54	-0.21 --	0.749

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED					
Dioxin Category	n	Adj. Mean[ae]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]	Covariate Remarks
Comparison	1,025	27.56			DRKYR (p=0.090) DC (p=0.049) AGE*ALC (p=0.001)
Background RH	362	26.25	-1.31 --	0.072	
Low RH	251	27.47	-0.09 --	0.913	
High RH	251	27.09	-0.47 --	0.581	
Low plus High RH	502	27.28	-0.28 --	0.667	

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not presented because analysis was performed on natural logarithm scale.

[d] P-value is based on difference of means on natural logarithm scale.

[e] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 13-14. (Continued)
Analysis of ALT (U/L)
(Continuous)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED						
	Current Dioxin Category Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)		
Model[b]	Low	Medium	High	R^2	Slope (Std. Error)[c]	p-Value
4	24.75 (290)	27.18 (298)	28.61 (296)	0.023	0.0476 (0.0104)	<0.001
5	24.96 (294)	26.82 (297)	28.82 (293)	0.025	0.0429 (0.0090)	<0.001
6[d]	25.12 (293)	26.83 (297)	28.66 (293)	0.025	0.0410 (0.0097)	<0.001

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED							
	Current Dioxin Category Adjusted Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)			
Model[b]	Low	Medium	High	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
4	23.86 (289)	26.68 (295)	27.82 (291)	0.070	0.0504 (0.0118)	<0.001	AGE (p<0.001) OCC (p<0.001) ALC (p=0.006) DC (p=0.003)
5	24.01 (292)	26.35 (295)	28.03 (288)	0.073	0.0450 (0.0099)	<0.001	AGE (p<0.001) OCC (p<0.001) ALC (p=0.007) DC (p=0.004)
6[e]	24.18 (291)	26.39 (295)	27.88 (288)	0.072	0.0434 (0.0108)	<0.001	AGE (p<0.001) OCC (p<0.001) ALC (p=0.008) DC (p=0.004)

[a] Transformed from natural logarithm scale.

[b] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for $\log_2$ total lipids.

[c] Slope and standard error based on natural logarithm of ALT versus $\log_2$ (current dioxin + 1).

[d] Adjusted for $\log_2$ total lipids.

[e] Adjusted for $\log_2$ total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

The adjusted results for Models 4, 5, and 6 paralleled the unadjusted results. All of the adjusted analyses uncovered a significant positive association between ALT and current dioxin (Table 13-14(h): $p<0.001$, Adj. Slope=0.0504; $p<0.001$, Adj. Slope=0.0450; and $p<0.001$, Adj. Slope=0.0434 for Models 4, 5, and 6 respectively). Each of the adjusted analyses for Models 4 through 6 contained age, occupation, current alcohol use, and degreasing chemical exposure.

ALT (Discrete)

The unadjusted Model 1 analysis did not find a significant group difference between the Ranch Hands and Comparisons in the proportion of ALT abnormalities (Table 13-15(a): $p>0.14$ for all contrasts).

The adjusted Model 1 analysis contained significant interactions between group and age and between group and degreasing chemical exposure (Table 13-15(b): $p=0.032$ and $p=0.011$ respectively). The results from analyzing ALT stratified by age and degreasing chemical exposure are displayed in Appendix Table I-2-6. The overall group contrast remained nonsignificant after removing these interactions from the final model (Table 13-15(b): $p=0.140$). However, stratifying the adjusted analysis by occupation revealed a marginally significant group difference within the enlisted groundcrew stratum (Table 13-15(b): $p=0.099$, Adj. RR=0.65, 95% C.I.=[0.38, 1.09]).

The unadjusted and adjusted analyses of Model 2 did not find a significant association between initial dioxin and ALT (Table 13-15(c,d): $p>0.17$ for both analyses). Current alcohol use was the only significant covariate in the adjusted analysis of Model 2.

The unadjusted Model 3 analysis did not reveal a significant association between categorized dioxin and ALT (Table 13-15(e): $p>0.11$ for all contrasts). Categorized dioxin-by-degreasing chemical exposure and categorized dioxin-by-current alcohol use interactions were significant in the adjusted analysis of Model 3 (Table 13-15(f): $p=0.006$ and $p=0.041$ respectively). Appendix Table I-2-6 presents adjusted results stratified separately by degreasing chemical exposure and current alcohol use. Besides these two interactions, the adjusted analysis also contained the age-by-current alcohol use interaction. After dropping the two categorized dioxin-by-covariate interactions, the adjusted analysis did not show a significant association between categorized dioxin and ALT (Table 13-15(f): $p>0.27$ for all contrasts).

The unadjusted analyses for Models 4 and 5 revealed a significant positive association between current dioxin and ALT (Table 13-15(g): $p=0.031$, Est. RR=1.24, 95% C.I.=[1.02, 1.50]; $p=0.017$, Est. RR=1.23, 95% C.I.=[1.04, 1.46] for Models 4 and 5 respectively). The unadjusted Model 6 analysis detected a marginally significant positive association between current dioxin and ALT (Table 13-15(g): $p=0.063$, Est. RR=1.19, 95% C.I.=[0.99, 1.43]).

The adjusted results for Models 4 through 6 paralleled the unadjusted results. The adjusted analyses of Models 4 and 5 revealed a significant positive association between current dioxin and ALT while the association was marginally significant in the adjusted

Table 13-15.
Analysis of ALT
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent High**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***939***	***5.5***	***0.76 (0.53,1.08)***	***0.144***
	Comparison	***1,253***	***7.2***		
Officer	Ranch Hand	361	5.8	0.96 (0.54,1.70)	0.998
	Comparison	495	6.1		
Enlisted Flyer	Ranch Hand	162	4.3	0.64 (0.25,1.63)	0.474
	Comparison	196	6.6		
Enlisted Groundcrew	Ranch Hand	416	5.8	0.67 (0.40,1.12)	0.155
	Comparison	562	8.4		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***0.77 (0.53,1.10)*****	***0.140*****	GROUP*AGE (p=0.032) GROUP*DC (p=0.011) RACE (p=0.036) ALC (p=0.001)
Officer	1.01 (0.56,1.80)**	0.979**	
Enlisted Flyer	0.68 (0.26,1.75)**	0.422**	
Enlisted Groundcrew	0.65 (0.38,1.09)**	0.099**	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

** Group-by-covariate interactions ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table I-2-6 for further analysis of these interactions.

Table 13-15. (Continued)
Analysis of ALT
(Discrete)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	173	2.3	1.17 (0.91,1.51)	0.221
Medium	170	8.8		
High	172	7.6		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
508	1.20 (0.93,1.55)	0.173	ALC (p<0.001)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 13-15. (Continued)
Analysis of ALT
(Discrete)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,043	7.0		
Background RH	369	4.1	0.63 (0.36,1.12)	0.117
Low RH	257	5.1	0.68 (0.37,1.26)	0.217
High RH	258	7.4	0.94 (0.55,1.60)	0.812
Low plus High RH	515	6.2	0.81 (0.52,1.26)	0.348

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,027			DXCAT*DC (p=0.006) DXCAT*ALC (p=0.041) AGE*ALC (p=0.014)
Background RH	367	0.72 (0.40,1.29)**	0.272**	
Low RH	254	0.71 (0.37,1.34)**	0.291**	
High RH	254	0.84 (0.49,1.45)**	0.538**	
Low plus High RH	508	0.78 (0.50,1.23)**	0.285**	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interactions ($p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table I-2-6 for further analysis of these interactions.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 13-15. (Continued)
Analysis of ALT
(Discrete)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent High/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	3.8 (290)	4.4 (298)	7.8 (296)	1.24 (1.02,1.50)	0.031
5	3.7 (294)	4.4 (297)	7.8 (293)	1.23 (1.04,1.46)	0.017
6[c]	3.8 (293)	4.4 (297)	7.8 (293)	1.19 (0.99,1.43)	0.063

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	875	1.30 (1.01,1.66)	0.035	OCC (p=0.058) DC (p<0.001) AGE (p=0.119) ALC (p=0.010)
5	875	1.28 (1.03,1.60)	0.024	OCC (p=0.050) DC (p<0.001) AGE (p=0.111) ALC (p=0.011)
6[d]	874	1.25 (0.99,1.59)	0.058	OCC (p=0.058) DC (p<0.001) AGE (p=0.104) ALC (p=0.013)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

analysis of Model 6 (Table 13-15(h): p=0.035, Adj. RR=1.30, 95% C.I.=[1.01, 1.66]; p=0.024, Adj. RR=1.28, 95% C.I.=[1.03, 1.60]; p=0.058, Adj. RR=1.25, 95% C.I.=[0.99, 1.59] for Models 4, 5, and 6 respectively]. Each of the three adjusted models accounted for occupation, degreasing chemical exposure, age, and current alcohol use.

A followup model excluding occupation was examined because of the high association between current dioxin levels and occupational categories. Removing occupation from Models 4, 5 and 6 caused the relative risk to become nonsignificant in each of the models. When occupation was removed from each of the adjusted analyses, current dioxin was no longer significantly associated with ALT (Appendix Table I-3-8: $p>0.16$ for all analyses).

GGT (Continuous)

The unadjusted and adjusted Model 1 analyses did not find a significant group difference in the mean level of GGT (Table 13-16(a,b): $p>0.17$ for all contrasts). The adjusted analysis contained race and three covariate-by-covariate interactions: age-by-occupation, age-by-industrial chemical exposure, and lifetime alcohol history-by-current alcohol use.

The unadjusted Model 2 results did not reveal a significant association between GGT and initial dioxin (Table 13-16(c): p=0.581). For the Model 2 adjusted analysis, the interaction between initial dioxin and degreasing chemical exposure was significant (Table 13-16(d): p=0.010). Appendix Table I-2-7 presents adjusted results stratified by degreasing chemical exposure. In addition to the interaction involving initial dioxin, the final model also contained occupation and two covariate-by-covariate interactions: age-by-lifetime alcohol history and age-by-current alcohol use. The adjusted analysis did not find a significant association between GGT and initial dioxin when the initial dioxin-by-degreasing chemical exposure interaction was removed from the final model (Table 13-16(d): p=0.177).

For Model 3, the unadjusted analysis detected a significant positive difference in the mean levels of GGT between the low plus high Ranch Hands and the Comparison group (Table 13-16(e): p=0.020). Further examination of contrasts involving the Comparisons revealed marginally significant increases for the low Ranch Hands and the high Ranch Hands (Table 13-16(e): p=0.085 and p=0.061 respectively). The mean levels of GGT for the low plus high Ranch Hands, high Ranch Hands, low Ranch Hands, and Comparisons were 34.58 U/L, 34.70 U/L, 34.47 U/L, and 31.97 U/L respectively.

The adjusted Model 3 analysis contained a significant interaction between categorized dioxin and degreasing chemical exposure (Table 13-16(f): p=0.034). The final model also included race and the lifetime alcohol history-by-current alcohol use interaction. Appendix Table I-2-7 displays adjusted results stratified by degreasing chemical exposure. The adjusted analysis uncovered two significant differences involving the Comparisons (low plus high Ranch Hands vs. Comparisons and high Ranch Hands vs. Comparisons) when the categorized dioxin-by-degreasing chemical exposure was removed from the analysis (Table 13-16(f): p=0.031 and p=0.011 respectively). The contrast between the low Ranch Hands and the Comparisons remained marginally significant in the adjusted analysis (Table 13-16(f): p=0.080).

Table 13-16.
Analysis of GGT (U/L)
(Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	*Ranch Hand*	*939*	*32.75*	*0.60 --*	*0.501*
	Comparison	*1,253*	*32.15*		
Officer	Ranch Hand	361	32.37	1.30 --	0.363
	Comparison	495	31.07		
Enlisted Flyer	Ranch Hand	162	31.43	-3.06 --	0.172
	Comparison	196	34.49		
Enlisted Groundcrew	Ranch Hand	416	33.61	1.29 --	0.332
	Comparison	562	32.32		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED						
Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]	Covariate Remarks[d]
All	*Ranch Hand*	*917*	*34.86*	*0.73 --*	*0.429*	RACE (p=0.014)
	Comparison	*1,232*	*34.13*			AGE*OCC (p=0.032)
Officer	Ranch Hand	357	33.70	0.80 --	0.571	AGE*IC (p=0.026)
	Comparison	487	32.90			DYKYR*ALC (p=0.004)
Enlisted Flyer	Ranch Hand	156	34.35	-1.40 --	0.545	
	Comparison	195	35.74			
Enlisted Groundcrew	Ranch Hand	404	35.80	1.44 --	0.305	
	Comparison	550	34.36			

[a] Transformed from natural logarithm scale.

[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

[c] P-values based on difference of means on natural logarithm scale.

[d] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 13-16. (Continued)
Analysis of GGT (U/L)
(Continuous)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	173	33.17	33.52	0.020	0.0117 (0.0212)	0.581
Medium	170	36.47	36.57			
High	172	35.98	35.51			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[d]			
Initial Dioxin	n	Adj. Mean[ad]	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
Low	170	33.67**	0.111	0.0329 (0.0243)**	0.177**	INIT*DC (p=0.010) OCC (p=0.028) AGE*DRKYR (p=0.015) AGE*ALC (p=0.024)
Medium	165	37.72**				
High	167	37.66**				

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Slope and standard error based on natural logarithm of GGT versus $\log_2$ (initial dioxin).

[d] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interaction ($p \leq 0.05$); adjusted mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-7 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 13-16. (Continued)
Analysis of GGT (U/L)
(Continuous)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED					
Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,043	32.01	31.97		
Background RH	369	29.33	30.12	-1.85 --	0.119
Low RH	257	34.70	34.47	2.50 --	0.085
High RH	258	35.64	34.70	2.73 --	0.061
Low plus High RH	515	35.17	34.58	2.61 --	0.020

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED					
Dioxin Category	n	Adj. Mean[ae]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]	Covariate Remarks
Comparison	1,025	34.34**			DXCAT*DC (p=0.034) RACE (p=0.008) DRKYR*ALC (p=0.002)
Background RH	362	32.60**	-1.75 --**	0.162**	
Low RH	251	36.99**	2.65 --**	0.080**	
High RH	251	37.67**	3.33 --**	0.031**	
Low plus High RH	502	37.33**	2.99 --**	0.011**	

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not presented because analysis was performed on natural logarithm scale.

[d] P-value is based on difference of means on natural logarithm scale.

[e] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted mean, difference of adjusted means, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-7 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 13-16. (Continued)
Analysis of GGT (U/L)
(Continuous)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[b]	Current Dioxin Category Mean[a]/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) R^2	Slope (Std. Error)[c]	p-Value
4	29.27 (290)	33.12 (298)	35.67 (296)	0.018	0.0578 (0.0142)	<0.001
5	28.88 (294)	32.83 (297)	36.57 (293)	0.027	0.0604 (0.0122)	<0.001
6[d]	30.13 (293)	32.96 (297)	34.91 (293)	0.051	0.0395 (0.0130)	0.002

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[b]	Current Dioxin Category Adjusted Mean[a]/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
4	28.87** (289)	33.02** (295)	35.84** (291)	0.088	0.0620 (0.0159)**	<0.001**	CURR*OCC (p=0.025) AGE (p=0.103) ALC (p<0.001)
5	28.48** (292)	32.59** (295)	36.92** (288)	0.097	0.0645 (0.0134)**	<0.001**	CURR*OCC (p=0.014) AGE (p=0.088) ALC (p<0.001)
6[e]	31.73** (291)	34.76** (295)	37.87** (288)	0.124	0.0448 (0.0144)**	0.002**	CURR*OCC (p=0.037) AGE (p=0.032) RACE (p=0.088) ALC*OCC (p=0.037)

[a] Transformed from natural logarithm scale.

[b] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for $\log_2$ total lipids.

[c] Slope and standard error based on natural logarithm of GGT versus $\log_2$ (current dioxin + 1).

[d] Adjusted for $\log_2$ total lipids.

[e] Adjusted for $\log_2$ total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-7 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

The unadjusted results for Models 4 through 6 showed a significant positive association between current dioxin and GGT (Table 13-16(g): $p<0.001$, Est. Slope=0.0578; $p<0.001$, Est. Slope=0.0604; $p=0.002$, Est. Slope=0.0395 for Models 4, 5, and 6 respectively). Each of the adjusted analyses for Models 4 through 6 contained a significant interaction between current dioxin and occupation (Table 13-16(h): $p=0.025$, $p=0.014$, $p=0.037$ for Models 4, 5, and 6 respectively). Appendix Table I-2-7 presents adjusted results stratified by occupation for each model. Models 4 and 5 also contained age and current alcohol use whereas Model 6 included age, race, and the current alcohol use-by-occupation interaction. The adjusted analyses for Models 4 through 6 revealed a significant positive association between current dioxin and GGT when the current dioxin-by-occupation interaction was removed from each of the final models (Table 13-16(h): $p<0.001$, Adj. Slope=0.0620; $p<0.001$, Adj. Slope=0.0645; $p=0.002$, Adj. Slope=0.0448).

GGT (Discrete)

The unadjusted and adjusted Model 1 analyses did not reveal a significant group difference in the proportion of GGT abnormalities (Table 13-17(a,b): $p>0.26$ for all contrasts). The adjusted model included age, race, and the current alcohol use-by-lifetime alcohol history interaction.

Unadjusted and adjusted analyses for Model 2 did not reveal a significant association between initial dioxin and GGT (Table 13-17(c,d): $p>0.57$ for both analyses). The adjusted analysis accounted for degreasing chemical exposure, current alcohol use, and an interaction between age and lifetime alcohol history.

For Model 3, the unadjusted analysis did not detect a significant contrast between Ranch Hand dioxin categories and the Comparison group (Table 13-17(e): $p>0.12$ for all contrasts). The adjusted Model 3 analysis contained a significant interaction between categorized dioxin and degreasing chemical exposure (Table 13-17(f): $p=0.008$). In addition to this interaction, the adjusted model also included age, and three other covariate-by-covariate interactions: race-by-current alcohol use, race-by-lifetime alcohol history, and current alcohol use-by-lifetime alcohol history. Appendix Table I-2-8 displays adjusted results stratified by degreasing chemical exposure. After removing the categorized dioxin-by-degreasing chemical exposure interaction from the final model, the adjusted analysis revealed a marginally significant relative risk for the low plus high Ranch Hands (Table 13-17(f): $p=0.070$, Adj. RR=1.29, 95% C.I.=[0.98, 1.70]).

The unadjusted analyses for Models 4 and 5 revealed a significant positive association between current dioxin and GGT (Table 13-17(g): $p=0.033$, Est. RR=1.13, 95% C.I.=[1.01, 1.26]; $p=0.009$, Est. RR=1.14, 95% C.I.=[1.03, 1.26]). The unadjusted Model 6 analysis was not significant ($p=0.131$).

All of the adjusted analyses for Models 4 through 6 contained a significant interaction between current dioxin and degreasing chemical exposure (Table 13-17(h): $p=0.005$, $p=0.015$, and $p=0.015$ for Models 4, 5, and 6 respectively). In addition, all three adjusted models accounted for age and the current alcohol use-by-lifetime alcohol history interaction. Appendix Table I-2-8 displays adjusted results stratified by degreasing chemical exposure.

Table 13-17.
Analysis of GGT
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent High**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***939***	***19.9***	***1.10 (0.89,1.36)***	***0.414***
	Comparison	***1,253***	***18.4***		
Officer	Ranch Hand	361	19.4	1.19 (0.84,1.70)	0.369
	Comparison	495	16.8		
Enlisted Flyer	Ranch Hand	162	17.9	0.82 (0.49,1.40)	0.560
	Comparison	196	20.9		
Enlisted Groundcrew	Ranch Hand	416	21.2	1.14 (0.83,1.56)	0.461
	Comparison	562	19.0		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.13 (0.91,1.42)***	***0.266***	AGE (p=0.006) RACE (p=0.091) ALC*DRKYR (p=0.010)
Officer	1.18 (0.82,1.70)	0.363	
Enlisted Flyer	0.96 (0.55,1.67)	0.891	
Enlisted Groundcrew	1.16 (0.84,1.61)	0.375	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 13-17. (Continued)
Analysis of GGT
(Discrete)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	173	17.3	1.05 (0.89,1.22)	0.574
Medium	170	26.5		
High	172	22.1		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
502	1.01 (0.85,1.20)	0.909	DC (p=0.010) ALC (p<0.001) AGE*DRKYR (p=0.018)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 13-17. (Continued)
Analysis of GGT
(Discrete)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	**n**	**Percent High**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,043	18.0		
Background RH	369	16.3	0.94 (0.68,1.30)	0.717
Low RH	257	21.4	1.22 (0.87,1.72)	0.249
High RH	258	22.5	1.24 (0.89,1.74)	0.201
Low plus High RH	515	21.9	1.23 (0.95,1.61)	0.120

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	**n**	**Adj. Relative Risk (95% C.I.)[ac]**	**p-Value**	**Covariate Remarks**
Comparison	1,025			DXCAT*DC (p=0.008) AGE (p=0.063) RACE*ALC (p=0.004) RACE*DRKYR (p=0.034) ALC*DRKYR (p=0.004)
Background RH	362	0.98 (0.70,1.38)**	0.920**	
Low RH	251	1.27 (0.89,1.81)**	0.191**	
High RH	251	1.31 (0.92,1.87)**	0.129**	
Low plus High RH	502	1.29 (0.98,1.70)**	0.070**	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interaction ($p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-8 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 13-17. (Continued)
Analysis of GGT
(Discrete)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent High/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	15.5 (290)	19.5 (298)	23.6 (296)	1.13 (1.01,1.26)	0.033
5	15.3 (294)	18.9 (297)	24.6 (293)	1.14 (1.03,1.26)	0.009
6[c]	15.4 (293)	18.9 (297)	24.6 (293)	1.09 (0.98,1.21)	0.131

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	864	1.14 (1.01,1.29)**	0.040**	CURR*DC (p=0.005) AGE (p=0.025) ALC*DRKYR (p=0.031)
5	864	1.15 (1.03,1.28)**	0.012**	CURR*DC (p=0.015) AGE (p=0.024) ALC*DRKYR (p=0.026)
6[d]	863	1.09 (0.97,1.23)**	0.133**	CURR*DC (p=0.015) AGE (p=0.012) ALC*DRKYR (p=0.033)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-8 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

The results from the adjusted analyses of Models 4 through 6 paralleled the unadjusted results when the current dioxin-by-degreasing chemical exposure interaction was removed from each of the final models. The adjusted analysis for Models 4 and 5 detected a significant positive association between GGT and current dioxin (Table 13-17(h): p=0.040, Adj. RR=1.14, 95% C.I.=[1.01, 1.29]; p=0.012, Adj. RR=1.15, 95% C.I.=[1.03, 1.28]). The adjusted Model 6 analysis was not significant (p=0.133).

Alkaline Phosphatase (Continuous)

The unadjusted Model 1 analysis of alkaline phosphatase detected a significant difference between the Ranch Hands and Comparisons (Table 13-18(a): p=0.005). The mean level of alkaline phosphatase was higher for the Ranch Hands than the Comparisons (70.73 U/L vs. 68.55 U/L). The unadjusted analysis also uncovered a significant group difference within the enlisted groundcrew stratum when the unadjusted analysis was stratified by occupation (Table 13-18(a): p=0.001). Among the enlisted groundcrew, the mean levels of alkaline phosphatase for the Ranch Hands and Comparisons were 73.35 U/L and 69.33 U/L respectively.

The adjusted Model 1 analysis contained three group-by-covariate interactions: group-by-age, group-by-race, and group-by-degreasing chemical exposure (Table 13-18(b): p=0.040, p=0.033, and p=0.017 respectively). Appendix Table I-2-9 presents adjusted results stratified separately by age, race, and degreasing chemical exposure. In addition to the three group-by-covariate interactions, the adjusted analysis included occupation and three covariate-by-covariate interactions: current wine use-by-degreasing chemical exposure, lifetime wine history-by-race, and lifetime wine history-by-degreasing chemical exposure. After removing the three group-by-covariate interactions from the final model, the adjusted analysis uncovered a significant overall group difference and a significant group difference within the enlisted groundcrew stratum (Table 13-18(b): p=0.005 and p=0.001 respectively).

The unadjusted Model 2 analysis did not find a significant association between initial dioxin and alkaline phosphatase (Table 13-18(c): p=0.547). The adjusted Model 2 analysis contained occupation and a significant interaction between initial dioxin and degreasing chemical exposure (Table 13-18(d): p=0.010). Appendix Table I-2-9 displays adjusted results stratified by degreasing chemical exposure. After removing the initial dioxin-by-degreasing chemical exposure interaction from the final model, the adjusted analysis did not find a significant association between initial dioxin and alkaline phosphatase (Table 13-18(d): p=0.422).

The unadjusted Model 3 results show three significant contrasts involving the Comparisons: low Ranch Hands versus Comparisons, high Ranch Hands versus Comparisons, and low plus high Ranch Hands versus Comparisons (Table 13-18(e): p=0.002, p=0.020, and p=0.001 respectively). The mean levels of alkaline phosphatase, adjusted for percent body fat at the time of duty in SEA and from the time of duty in SEA to the date of the blood draw for dioxin, for the low Ranch Hands, high Ranch Hands, low plus high Ranch Hands, and Comparisons were 72.13 U/L, 71.24 U/L, 71.69 U/L, and 68.34 U/L respectively.

Table 13-18.
Analysis of Alkaline Phosphatase (U/L)
(Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Mean[a]**	**Difference of Means (95% C.I.)[b]**	**p-Value[c]**
All	*Ranch Hand*	*939*	*70.73*	*2.18 --*	*0.005*
	Comparison	*1,253*	*68.55*		
Officer	Ranch Hand	361	67.74	1.18 --	0.329
	Comparison	495	66.56		
Enlisted Flyer	Ranch Hand	162	70.93	-0.53 --	0.790
	Comparison	196	71.45		
Enlisted Groundcrew	Ranch Hand	416	73.35	4.02 --	0.001
	Comparison	562	69.33		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED						
Occupational Category	**Group**	**n**	**Adj. Mean[a]**	**Difference of Adj. Means (95% C.I.)[b]**	**p-Value[c]**	**Covariate Remarks[d]**
All	*Ranch Hand*	*920*	*71.05***	*2.20 --***	*0.005***	GROUP*AGE (p=0.040)
	Comparison	*1,232*	*68.85***			GROUP*RACE (p=0.033)
Officer	Ranch Hand	357	67.51**	1.43 --**	0.231**	GROUP*DC (p=0.017)
	Comparison	487	66.08**			OCC (p<0.001)
						WINE*DC (p=0.013)
Enlisted Flyer	Ranch Hand	157	70.53**	-0.54 --**	0.782**	LWINE*RACE (p=0.007)
	Comparison	195	71.07**			LWINE*DC (p=0.014)
Enlisted Groundcrew	Ranch Hand	406	74.24**	3.95 --**	0.001**	
	Comparison	550	70.29**			

[a] Transformed from natural logarithm scale.

[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

[c] P-values based on difference of means on natural logarithm scale.

[d] Covariates and associated p-values correspond to final model based on all participants with available data.

** Group-by-covariate interactions (0.01<p≤0.05); adjusted mean, difference of adjusted means, confidence interval, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table I-2-9 for further analysis of these interactions.

Table 13-18. (Continued)
Analysis of Alkaline Phosphatase (U/L)
(Continuous)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				**Analysis Results for Log_2 (Initial Dioxin)[b]**		
Initial Dioxin	**n**	**Mean[a]**	**Adj. Mean[ab]**	**R^2**	**Slope (Std. Error)[c]**	**p-Value**
Low	173	70.40	70.57	0.009	0.0050 (0.0083)	0.547
Medium	170	72.85	72.95			
High	172	72.26	71.99			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)[d]**			
Initial Dioxin	**n**	**Adj. Mean[ad]**	**R^2**	**Adj. Slope (Std. Error)[c]**	**p-Value**	**Covariate Remarks**
Low	173	70.43**	0.038	-0.0076 (0.0094)**	0.422**	INIT*DC (p=0.010) OCC (p=0.139)
Medium	170	71.46**				
High	172	69.12**				

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Slope and standard error based on natural logarithm of alkaline phosphatase versus $\log_2$ (initial dioxin).

[d] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted means, adjusted slope, standard error, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-9 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 13-18. (Continued)
Analysis of Alkaline Phosphatase (U/L)
(Continuous)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,043	68.35	68.34		
Background RH	369	69.32	69.53	1.20 --	0.267
Low RH	257	72.19	72.13	3.80 --	0.002
High RH	258	71.45	71.24	2.90 --	0.020
Low plus High RH	515	71.82	71.69	3.35 --	0.001

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Mean[ae]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]	Covariate Remarks
Comparison	1,027	67.48**			DXCAT*DC (p=0.012) AGE (p<0.001) OCC (p<0.001) WINE (p=0.022) RACE*IC (p=0.002)
Background RH	366	69.68**	2.20 --**	0.043**	
Low RH	254	70.87**	3.38 --**	0.006**	
High RH	254	68.96**	1.47 --**	0.239**	
Low plus High RH	508	69.90**	2.42 --**	0.011**	

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not presented because analysis was performed on natural logarithm scale.

[d] P-value is based on difference of means on natural logarithm scale.

[e] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interaction ($p \leq 0.05$); adjusted mean, difference of adjusted means, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-9 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 13-18. (Continued)
Analysis of Alkaline Phosphatase (U/L)
(Continuous)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

	Current Dioxin Category Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)		
Model[b]	Low	Medium	High	R^2	Slope (Std. Error)[c]	p-Value
4	69.50 (290)	70.91 (298)	71.89 (296)	0.001	0.0063 (0.0059)	0.286
5	69.86 (294)	70.13 (297)	72.35 (293)	0.001	0.0056 (0.0050)	0.266
6[d]	70.29 (293)	70.18 (297)	71.79 (293)	0.007	0.0024 (0.0054)	0.665

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

	Current Dioxin Category Adjusted Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)			
Model[b]	Low	Medium	High	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
4	67.94** (287)	68.61** (291)	66.36** (289)	0.045	-0.0100 (0.0067)**	0.136**	CURR*RACE (p=0.040) AGE (p=0.050) OCC (p=0.139) LWINE (p=0.015) DC (p=0.102)
5	68.29** (290)	67.80** (291)	67.08** (286)	0.046	-0.0078 (0.0057)**	0.167**	CURR*RACE (p=0.020) AGE (p=0.044) OCC (p<0.001) LWINE (p=0.014) DC (p=0.105)
6[e]	68.92** (289)	68.02** (291)	66.64** (286)	0.051	-0.0118 (0.0061)**	0.054**	CURR*RACE (p=0.017) AGE (p=0.072) OCC (p<0.001) LWINE (p=0.017) DC (p=0.131)

[a] Transformed from natural logarithm scale.

[b] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[c] Slope and standard error based on natural logarithm of alkaline phosphatase versus log_2 (current dioxin + 1).

[d] Adjusted for log_2 total lipids.

[e] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-9 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

The adjusted Model 3 analysis contained a significant interaction between categorized dioxin and degreasing chemical exposure (Table 13-18(f): p=0.012). Appendix Table I-2-9 presents adjusted results stratified by degreasing chemical exposure. In addition to the categorized dioxin-by-degreasing chemical exposure interaction, the adjusted analysis for Model 3 included age, occupation, current wine use, and the interaction between race and industrial chemical exposure. The adjusted analysis detected three significant contrasts when the categorized dioxin-by-degreasing chemical exposure interaction was removed from the final model. The contrasts for the low Ranch Hands and low plus high Ranch Hands remained significant in the adjusted analysis (Table 13-18(f): p=0.006 and p=0.011 respectively), and the background Ranch Hand contrasts became significant in the adjusted analysis (Table 13-18(f): p=0.043). The high Ranch Hand contrast was nonsignificant in the adjusted analysis (p=0.239).

Removing occupation from the Model 3 analysis produced a change in the adjusted results. When occupation and the categorized dioxin-by-degreasing chemical exposure interaction were removed from the final model, the adjusted results were similar to the unadjusted results. This adjusted analysis did not find a significant difference between the background Ranch Hands and the Comparisons. The contrasts for the low Ranch Hands, high Ranch Hands, and low plus high Ranch Hands were significant (Appendix Table I-3-10(b): p=0.006, p=0.024, and p=0.001 respectively).

The unadjusted analyses of Models 4 through 6 did not reveal a significant association between current dioxin and alkaline phosphatase (Table 13-18(g): p>0.26 for all analyses). Each of the adjusted analyses for Models 4 through 6 contained a significant interaction between current dioxin and race (Table 13-18(h): p=0.040, p=0.020, and p=0.017 for Models 4, 5, and 6). In addition to this interaction, all of the adjusted models contained age, occupation, lifetime wine history, and degreasing chemical exposure. For Models 4 through 6, Appendix Table I-2-9 presents adjusted results stratified by race. After removing the current dioxin-by-race interaction from Models 4 through 6, the adjusted analyses of Models 4 and 5 did not show a significant association between alkaline phosphatase and current dioxin (Table 13-18(h): p>0.13 for both analyses). However, the adjusted Model 6 analysis revealed a marginally significant negative association between current dioxin and alkaline phosphatase (Table 13-18(h): p=0.054).

The adjusted results for Models 4 through 6 resembled the unadjusted results when occupation was removed from each of the final models. Without occupation, the adjusted analyses for Models 4 through 6 did not indicate a significant association between alkaline phosphatase and current dioxin (Appendix Table I-3-10(c): p>0.55 for all analyses).

Alkaline Phosphatase (Discrete)

The unadjusted Model 1 analysis detected a significant group difference in the proportion of alkaline phosphatase abnormalities (Table 13-19(a): p=0.039, Est. RR=1.59, 95% C.I.=[1.04, 2.42]). Ranch Hands were more likely than Comparisons to have abnormally high levels of alkaline phosphatase (5.2% vs. 3.4%). Stratifying the unadjusted analysis by occupation revealed a significant difference between the Ranch Hand and Comparison enlisted groundcrew strata (Table 13-19(a): p=0.007, Est. RR=2.26, 95%

Table 13-19.
Analysis of Alkaline Phosphatase
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Percent High	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***939***	***5.2***	***1.59 (1.04,2.42)***	***0.039***
	Comparison	***1,253***	***3.4***		
Officer	Ranch Hand	361	2.8	1.06 (0.46,2.44)	0.999
	Comparison	495	2.6		
Enlisted Flyer	Ranch Hand	162	4.3	0.94 (0.34,2.58)	0.999
	Comparison	196	4.6		
Enlisted Groundcrew	Ranch Hand	416	7.7	2.26 (1.27,4.01)	0.007
	Comparison	562	3.6		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	***1.49 (0.97,2.29)***	***0.072***	AGE (p<0.001)
Officer	1.03 (0.45,2.39)	0.941	OCC (p=0.001)
Enlisted Flyer	0.81 (0.28,2.34)	0.699	DC*LWINE (p=0.049)
Enlisted Groundcrew	2.14 (1.19,3.84)	0.011	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 13-19. (Continued)
Analysis of Alkaline Phosphatase
(Discrete)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	173	3.5	1.07 (0.81,1.41)	0.631
Medium	170	6.5		
High	172	5.8		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
504	0.93 (0.67,1.31)**	0.695**	INIT*IC (p=0.030) AGE (p=0.134) OCC*LWINE (p=0.021)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-10 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 13-19. (Continued)
Analysis of Alkaline Phosphatase
(Discrete)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	**n**	**Percent High**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,043	3.1		
Background RH	369	4.9	1.68 (0.92,3.05)	0.089
Low RH	257	5.8	1.86 (0.99,3.50)	0.055
High RH	258	4.7	1.50 (0.76,2.97)	0.247
Low plus High RH	515	5.2	1.68 (0.99,2.85)	0.054

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	**n**	**Adj. Relative Risk (95% C.I.)[ac]**	**p-Value**	**Covariate Remarks**
Comparison	1,043			AGE (p=0.006) OCC (p<0.001)
Background RH	369	1.98 (1.07,3.67)	0.030	
Low RH	257	1.85 (0.98,3.51)	0.059	
High RH	258	1.26 (0.63,2.54)	0.516	
Low plus High RH	515	1.54 (0.90,2.63)	0.112	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 13-19. (Continued)
Analysis of Alkaline Phosphatase
(Discrete)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category Percent High/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) Est. Relative Risk (95% C.I.)[b]	p-Value
4	3.4 (290)	6.0 (298)	5.7 (296)	1.03 (0.84,1.27)	0.762
5	4.1 (294)	5.7 (297)	5.5 (293)	1.03 (0.86,1.22)	0.776
6[c]	4.1 (293)	5.7 (297)	5.5 (293)	0.97 (0.80,1.18)	0.764

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[a]	Analysis Results for Log_2 (Current Dioxin + 1) n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	884	0.90 (0.73,1.12)	0.360	AGE ($p=0.058$) OCC ($p<0.001$)
5	884	0.92 (0.77,1.10)	0.374	AGE ($p=0.055$) OCC ($p<0.001$)
6[d]	883	0.86 (0.71,1.05)	0.148	AGE ($p=0.076$) OCC ($p<0.001$)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

C.I.=[1.27, 4.01]). The percentage of abnormalities was higher for the Ranch Hands than for the Comparisons (7.7% vs. 3.6%).

In the adjusted Model 1 analysis, the overall group contrast became marginally significant, and the group contrast within the enlisted groundcrew stratum remained significant (Table 13-19(b): p=0.072, Adj. RR=1.49, 95% C.I.=[0.97, 2.29]; p=0.011, Adj. RR=2.14, 95% C.I.=[1.19, 4.01] respectively). The final adjusted model contained age, occupation, and the interaction between degreasing chemical exposure and lifetime wine history.

The unadjusted Model 2 results did not reveal a significant association between alkaline phosphatase and initial dioxin (Table 13-19(c): p=0.631). The adjusted analysis contained a significant interaction between initial dioxin and industrial chemical exposure (Table 13-19(d): p=0.030). In addition to this interaction, the adjusted model also included age and the occupation-by-lifetime wine history interaction. Appendix Table I-2-10 presents adjusted results stratified by industrial chemical exposure. The adjusted analysis did not find a significant association between alkaline phosphatase and initial dioxin when the initial dioxin-by-industrial chemical exposure interaction was removed from the final model (Table 13-19(d): p=0.695).

Examination of the unadjusted Model 3 results revealed marginally significant relative risks greater than one for each Ranch Hand category other than the high Ranch Hand category: (Table 13-19(e): p=0.089, Est. RR=1.68, 95% C.I.=[0.92, 3.05] for the background Ranch Hands; p=0.055, Est. RR=1.86, 95% C.I.=[0.99, 3.50] for the low Ranch Hands; and p=0.054, Est. RR=1.68, 95% C.I.=[0.99, 2.85] for the low plus high Ranch Hands). The percentages of alkaline phosphatase abnormalities for the background Ranch Hands, low Ranch Hands, low plus high Ranch Hands, and the Comparison group were 4.9 percent, 5.8 percent, 5.2 percent, and 3.1 percent respectively.

After adjusting for age and occupation, the relative risk for the background Ranch Hands became significant, and the relative risk for the low Ranch Hands remained marginally significant (Table 13-19(f): p=0.030, Adj. RR=1.98, 95% C.I.=[1.07, 3.67]); p=0.059, Adj. RR=1.85, 95% C.I.=[0.98, 3.51] respectively). For the low plus high Ranch Hand category, the relative risk became nonsignificant (Table 13-19(f): p=0.112).

Results from the adjusted analysis changed when occupation was removed from Model 3. Without occupation, the adjusted analysis detected a significant relative risk for the low plus high Ranch Hands and a marginally significant relative risk for the low Ranch Hands (Appendix Table I-3-11(b): p=0.047, Adj. RR=1.71, 95% C.I.=[1.01, 2.91]; p=0.070, Adj. RR=1.80, 95% C.I.=[0.95, 3.39] respectively). The background Ranch Hands and Comparisons were not significantly different in this analysis (Appendix Table I-3-11(b): p=0.111).

The unadjusted and adjusted analyses for Models 4 through 6 did not detect a significant association between alkaline phosphatase and current dioxin (Table 13-19(g,h): p>0.14 for all analyses). The adjusted model contained age and occupation.

Total Bilirubin (Continuous)

The unadjusted and adjusted Model 1 results did not reveal a significant group difference in the mean levels of total bilirubin (Table 13-20(a,b): $p>0.16$ for all contrasts). The adjusted Model 1 analysis included occupation, current alcohol use, and the age-by-industrial chemical exposure interaction.

For Model 2, the unadjusted and adjusted analyses did not reveal a significant association between total bilirubin and initial dioxin (Table 13-20(c,d): $p>0.37$ for both analyses). Occupation was the only significant covariate in Model 2.

The unadjusted Model 3 analysis revealed a significant and a marginally significant negative contrast for the high Ranch Hands and the low plus high Ranch Hands respectively (Table 13-20(e): $p=0.033$ and $p=0.080$). The mean levels of total bilirubin, adjusted for percent body fat at the time of duty in SEA and the change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, for the high Ranch Hands, low plus high Ranch Hands, and Comparisons were 0.59 mg/dl, 0.61 mg/dl, and 0.63 mg/dl respectively.

The adjusted analysis of Model 3 did not reveal a significant contrast involving the Comparisons (Table 13-20(f): $p>0.11$ for all contrasts). The adjusted analysis included age, occupation, and current alcohol use. Results from the adjusted model changed slightly when occupation was removed from the analysis. Without occupation, the adjusted Model 3 analysis revealed a marginally significant negative difference between the high Ranch Hand category and the Comparison group (Appendix Table I-3-12(a): $p=0.074$).

The unadjusted analyses for Models 4 through 6 did not show a significant association between total bilirubin and current dioxin (Table 13-20(g): $p>0.28$ for all analyses). For Model 4, the adjusted analysis contained a significant interaction between current dioxin and degreasing chemical exposure (Table 13-20(h): $p=0.048$). Appendix Table I-2-11 presents adjusted results stratified by degreasing chemical exposure. The adjusted analysis for Model 4 also contained occupation and the age-by-race interaction. After removing the interaction between current dioxin and degreasing chemical exposure from the final model, the adjusted Model 4 analysis did not reveal a significant association between total bilirubin and current dioxin (Table 13-20(h): $p=0.774$).

The adjusted analyses for Models 5 and 6 did not indicate a significant association between total bilirubin and current dioxin (Table 13-20(h): $p>0.46$ for both analyses). Both of the adjusted models contained occupation and the age-by-race interaction.

Total Bilirubin (Discrete)

The unadjusted and adjusted Model 1 analyses did not reveal a significant group difference in the percentage of total bilirubin abnormalities (Table 13-21(a,b): $p>0.54$ for all contrasts). The adjusted model contained the current alcohol use-by-lifetime alcohol history interaction.

Table 13-20.
Analysis of Total Bilirubin (mg/dl)
(Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Mean**[a]	**Difference of Means (95% C.I.)**[b]	**p-Value**[c]
All	***Ranch Hand***	***939***	***0.62***	***-0.01 --***	***0.469***
	Comparison	***1,253***	***0.63***		
Officer	Ranch Hand	361	0.65	0.01 --	0.593
	Comparison	495	0.64		
Enlisted Flyer	Ranch Hand	162	0.58	-0.04 --	0.161
	Comparison	196	0.61		
Enlisted Groundcrew	Ranch Hand	416	0.62	-0.01 --	0.561
	Comparison	562	0.63		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED						
Occupational Category	**Group**	**n**	**Adj. Mean**[a]	**Difference of Adj. Means (95% C.I.)**[b]	**p-Value**[c]	**Covariate Remarks**[d]
All	***Ranch Hand***	***929***	***0.61***	***-0.01 --***	***0.600***	OCC (p=0.022)
	Comparison	***1,235***	***0.62***			ALC (p<0.001)
Officer	Ranch Hand	361	0.64	0.01 --	0.645	AGE*IC (p=0.030)
	Comparison	488	0.63			
Enlisted Flyer	Ranch Hand	159	0.58	-0.03 --	0.221	
	Comparison	196	0.61			
Enlisted Groundcrew	Ranch Hand	409	0.62	-0.01 --	0.637	
	Comparison	551	0.63			

[a] Transformed from natural logarithm scale.

[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

[c] P-values based on difference of means on natural logarithm scale.

[d] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 13-20. (Continued)
Analysis of Total Bilirubin (mg/dl)
(Continuous)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	173	0.65	0.65	0.005	-0.0125 (0.0140)	0.374
Medium	170	0.59	0.59			
High	172	0.60	0.60			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[d]			
Initial Dioxin	n	Adj. Mean[ad]	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
Low	173	0.64	0.020	0.0013 (0.0159)	0.934	OCC (p=0.021)
Medium	170	0.59				
High	172	0.61				

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Slope and standard error based on natural logarithm of total bilirubin versus $\log_2$ (initial dioxin).

[d] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 13-20. (Continued)
Analysis of Total Bilirubin (mg/dl)
(Continuous)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED					
Dioxin Category	**n**	**Mean[a]**	**Adj. Mean[ab]**	**Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]**	**p-Value[d]**
Comparison	1,043	0.63	0.63		
Background RH	369	0.63	0.64	0.01 --	0.721
Low RH	257	0.62	0.62	-0.01 --	0.561
High RH	258	0.60	0.59	-0.04 --	0.033
Low plus High RH	515	0.61	0.61	-0.02 --	0.080

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED					
Dioxin Category	**n**	**Adj. Mean[ae]**	**Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]**	**p-Value[d]**	**Covariate Remarks**
Comparison	1,027	0.62			AGE (p=0.058) OCC (p=0.084) ALC (p<0.001)
Background RH	367	0.63	0.00 --	0.888	
Low RH	254	0.62	-0.01 --	0.700	
High RH	254	0.60	-0.03 --	0.114	
Low plus High RH	508	0.61	-0.02 --	0.198	

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not presented because analysis was performed on natural logarithm scale.

[d] P-value is based on difference of means on natural logarithm scale.

[e] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 13-20. (Continued)
Analysis of Total Bilirubin (mg/dl)
(Continuous)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[b]	Current Dioxin Category Mean[a]/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) R^2	Slope (Std. Error)[c]	p-Value
4	0.63 (290)	0.64 (298)	0.59 (296)	0.001	-0.0088 (0.0093)	0.343
5	0.63 (294)	0.63 (297)	0.60 (293)	<0.001	-0.0041 (0.0080)	0.607
6[d]	0.64 (293)	0.63 (297)	0.59 (293)	0.003	-0.0093 (0.0086)	0.281

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[b]	Current Dioxin Category Adjusted Mean[a]/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
4	0.61** (290)	0.63** (298)	0.59** (296)	0.022	0.0031 (0.0106)**	0.774**	CURR*DC (p=0.048) OCC (p=0.007) AGE*RACE (p=0.029)
5	0.61 (294)	0.62 (297)	0.61 (293)	0.017	0.0065 (0.0090)	0.469	OCC (p=0.011) AGE*RACE (p=0.027)
6[e]	0.62 (293)	0.62 (297)	0.60 (293)	0.019	0.0019 (0.0097)	0.847	OCC (p=0.015) AGE*RACE (p=0.032)

[a] Transformed from natural logarithm scale.

[b] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[c] Slope and standard error based on natural logarithm of total bilirubin versus log_2 (current dioxin + 1).

[d] Adjusted for log_2 total lipids.

[e] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-11 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 13-21.
Analysis of Total Bilirubin
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent High**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***939***	***5.1***	***1.07 (0.73,1.58)***	***0.805***
	Comparison	***1,253***	***4.8***		
Officer	Ranch Hand	361	5.8	1.11 (0.62,2.01)	0.837
	Comparison	495	5.3		
Enlisted Flyer	Ranch Hand	162	3.1	0.75 (0.24,2.33)	0.828
	Comparison	196	4.1		
Enlisted Groundcrew	Ranch Hand	416	5.3	1.15 (0.64,2.06)	0.746
	Comparison	562	4.6		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.10 (0.74,1.63)***	***0.632***	ALC*DRKYR (p=0.015)
Officer	1.12 (0.62,2.03)	0.702	
Enlisted Flyer	0.78 (0.25,2.45)	0.674	
Enlisted Groundcrew	1.20 (0.66,2.16)	0.549	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 13-21. (Continued)
Analysis of Total Bilirubin
(Discrete)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	173	6.9	0.97 (0.71,1.33)	0.844
Medium	170	2.4		
High	172	4.7		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
502	0.88 (0.64,1.22)**	0.449**	INIT*IC (p=0.026) DC (p=0.004) RACE*DRKYR (p=0.019) ALC*DRKYR (p=0.009)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-12 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 13-21. (Continued)
Analysis of Total Bilirubin
(Discrete)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	**n**	**Percent High**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,043	5.0		
Background RH	369	5.4	1.12 (0.65,1.91)	0.682
Low RH	257	4.7	0.92 (0.48,1.75)	0.795
High RH	258	4.7	0.92 (0.48,1.75)	0.788
Low plus High RH	515	4.7	0.92 (0.56,1.51)	0.732

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	**n**	**Adj. Relative Risk (95% C.I.)[ac]**	**p-Value**	**Covariate Remarks**
Comparison	1,025			ALC*DRKYR (p=0.014)
Background RH	362	1.17 (0.68,2.00)	0.572	
Low RH	251	0.97 (0.51,1.86)	0.934	
High RH	251	0.90 (0.47,1.73)	0.753	
Low plus High RH	502	0.94 (0.57,1.55)	0.796	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 13-21. (Continued)
Analysis of Total Bilirubin
(Discrete)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent High/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	5.5 (290)	5.4 (298)	4.1 (296)	0.94 (0.76,1.16)	0.550
5	5.4 (294)	4.7 (297)	4.8 (293)	0.97 (0.81,1.16)	0.768
6[c]	5.5 (293)	4.7 (297)	4.8 (293)	0.92 (0.76,1.12)	0.415

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	875	0.93 (0.75,1.16)**	0.527**	CURR*DC (p=0.020) IC (p=0.066) AGE*ALC (p=0.015)
5	875	0.97 (0.81,1.17)**	0.776**	CURR*DC (p=0.024) IC (p=0.067) AGE*ALC (p=0.017)
6[d]	874	0.92 (0.75,1.12)**	0.388**	CURR*DC (p=0.024) IC (p=0.057) DC*ALC (p=0.050) AGE*ALC (p=0.013)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-12 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

For Model 2, the unadjusted analysis did not reveal a significant association between total bilirubin and initial dioxin (Table 13-21(c): p=0.844). The adjusted Model 2 analysis detected a significant interaction between initial dioxin and industrial chemical exposure (Table 13-21(d): p=0.026). Appendix Table I-2-12 presents adjusted results stratified by industrial chemical exposure. The adjusted analysis contained degreasing chemical exposure and two covariate-by-covariate interactions: race-by-lifetime alcohol history and current alcohol use-by-lifetime alcohol history. The adjusted analysis of Model 2 did not reveal a significant association between total bilirubin and initial dioxin when the initial dioxin-by-industrial chemical exposure interaction was removed from the final model (Table 13-21(d): p=0.449).

The unadjusted and adjusted Model 3 results did not show any of the four Ranch Hand categories to be significantly different from the Comparison group (Table 13-21(e,f): p>0.57 for all contrasts). The adjusted model contained an interaction between current alcohol use and lifetime alcohol history.

The unadjusted analyses for Models 4 through 6 did not reveal a significant association between total bilirubin and current dioxin (Table 13-21(g): p>0.41 for all analyses). Each of the adjusted analyses contained a significant interaction between current dioxin and degreasing chemical exposure (Table 13-21(h): p=0.020, p=0.024, and p=0.024 for Models 4, 5, and 6 respectively). Appendix Table I-2-12 presents adjusted results stratified by degreasing chemical exposure for Models 4 through 6. Besides the current dioxin-by-degreasing chemical interaction, the adjusted analyses for Models 4 and 5 contained industrial chemical exposure and the age-by-current alcohol use interaction. Model 6 contained industrial chemical exposure, the degreasing chemical exposure-by-current alcohol use interaction, and the age-by-current alcohol use interaction. The adjusted analyses for Models 4 through 6 did not reveal a significant association between total bilirubin and current dioxin when the current dioxin-by-degreasing chemical exposure interaction was removed from each of the final models (Table 13-12(h): p>0.38 for all analyses).

Direct Bilirubin

The unadjusted Model 1 analysis did not show a significant overall group difference in the percentage of direct bilirubin abnormalities (Table 13-22(a): p=0.127). However, stratifying the analysis by occupation revealed a significant group difference within the enlisted groundcrew stratum (Table 13-22(a): p=0.022, Est. RR=0.23, 95% C.I.=[0.07, 0.80]. Among the enlisted groundcrew, Ranch Hands had a significantly lower percentage of abnormalities than Comparisons (0.7% vs. 3.0%).

After adjusting for occupation and the current alcohol use-by-industrial chemical exposure interaction, the adjusted Model 1 analysis did not show a significant difference between Ranch Hands and Comparisons (Table 13-22(b): p=0.111). Similar to the unadjusted analysis, the stratified adjusted analysis revealed a significant group difference within the enlisted groundcrew stratum (Table 13-22(b): p=0.026, Adj. RR=0.24, 95% C.I.=[0.07, 0.84]).

Table 13-22.
Analysis of Direct Bilirubin

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent High**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***938***	***1.4***	***0.57 (0.30,1.10)***	***0.127***
	Comparison	***1,253***	***2.4***		
Officer	Ranch Hand	361	2.5	1.13 (0.46,2.74)	0.976
	Comparison	495	2.2		
Enlisted Flyer	Ranch Hand	161	0.6	0.61 (0.05,6.75)	0.999
	Comparison	196	1.0		
Enlisted Groundcrew	Ranch Hand	416	0.7	0.23 (0.07,0.80)	0.022
	Comparison	562	3.0		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***0.59 (0.31,1.15)***	***0.111***	OCC (p=0.060) ALC*IC (p=0.042)
Officer	1.12 (0.46,2.73)	0.810	
Enlisted Flyer	0.67 (0.06,7.53)	0.742	
Enlisted Groundcrew	0.24 (0.07,0.84)	0.026	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 13-22. (Continued)
Analysis of Direct Bilirubin

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	173	2.3	0.73 (0.36,1.46)	0.348
Medium	170	0.0		
High	172	1.2		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
	Analysis Results for Log_2 (Initial Dioxin)[a]		
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
515	0.73 (0.36,1.46)	0.348	

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 13-22. (Continued)
Analysis of Direct Bilirubin

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,043	2.3		
Background RH	369	1.4	0.71 (0.27,1.91)	0.503
Low RH	257	1.6	0.61 (0.21,1.78)	0.363
High RH	258	0.8	0.27 (0.06,1.16)	0.078
Low plus High RH	515	1.2	0.43 (0.17,1.07)	0.069

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,027			OCC (p=0.048) IC (p=0.011) RACE*AGE (p=0.035) AGE*ALC (p=0.039)
Background RH	367	0.67 (0.24,1.86)	0.441	
Low RH	254	0.62 (0.21,1.89)	0.403	
High RH	254	0.34 (0.08,1.49)	0.151	
Low plus High RH	508	0.49 (0.19,1.23)	0.127	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 13-22. (Continued)
Analysis of Direct Bilirubin

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent High/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	1.0 (290)	2.0 (298)	0.7 (296)	0.86 (0.56,1.32)	0.488
5	0.3 (294)	2.4 (297)	1.0 (293)	1.00 (0.70,1.42)	0.990
6[c]	0.3 (293)	2.4 (297)	1.0 (293)	0.70 (0.48,1.02)	0.075

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	864	1.19 (0.68,2.11)**	0.539**	CURR*DRKYR (p=0.028) OCC (p=0.028)
5	864	1.42 (0.86,2.35)**	0.156**	CURR*DRKYR (p=0.004) OCC (p=0.004)
6[d]	863	0.88 (0.54,1.44)**	0.621**	CURR*DRKYR (p=0.039) OCC (p=0.045)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-13 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

The unadjusted Model 2 results did not show a significant association between direct bilirubin and initial dioxin (Table 13-22(c): $p=0.348$). The adjusted results were identical to the unadjusted results because no covariates were retained in the final model.

The unadjusted Model 3 analysis revealed two marginally significant contrasts: high Ranch Hands versus Comparisons and low plus high Ranch Hands versus Comparisons (Table 13-22(e): $p=0.078$, Est. RR=0.27, 95% C.I.=[0.06, 1.16]; $p=0.069$, Est. RR=0.43, 95% C.I.=[0.17, 1.07]). The percentages of individuals with high levels of direct bilirubin among high Ranch Hands, low plus high Ranch Hands, and Comparisons were 0.8 percent, 1.2 percent, and 2.3 percent respectively.

After covariate adjustment, the Model 3 analysis did not show any of the Ranch Hand categories to be significantly different from the Comparison group (Table 13-22(f): $p>0.12$ for all contrasts). The adjusted model contained occupation, industrial chemical exposure, and two covariate-by-covariate interactions: race-by-age and age-by-current alcohol use. The results of the adjusted Model 3 analysis without occupation resembled the unadjusted results. Excluding occupation, the adjusted analysis revealed two marginally significant contrasts, high Ranch Hands versus Comparisons and low plus high Ranch Hands versus the Comparison group (Appendix Table I-3-13: $p=0.079$ and $p=0.083$ respectively).

The unadjusted analyses of Models 4 and 5 did not indicate a significant association between direct bilirubin and current dioxin (Table 13-22(g): $p>0.48$ for both analyses). However, the unadjusted Model 6 analysis detected a marginally negative significant association (Table 13-22(g): $p=0.075$, Est. RR=0.70, 95% C.I.=[0.48, 1.02]).

Each of the adjusted analyses for Models 4 through 6 contained a significant interaction between current alcohol use and lifetime alcohol history (Table 13-22(h): $p=0.028$, $p=0.004$, and $p=0.039$ for Models 4, 5, and 6 respectively). Appendix Table I-2-13 presents adjusted results stratified by lifetime alcohol history for Models 4 through 6. In addition to the current dioxin-by-lifetime alcohol history interaction, the adjusted analyses for Models 4 through 6 contained occupation. None of the adjusted analyses showed a significant association between direct bilirubin and current dioxin when the current dioxin-by-lifetime alcohol history interaction was removed from the final model (Table 13-22(h): $p>0.15$ for each analysis).

Removing occupation from the adjusted analyses of Models 4 through 6 changed the results only for Model 6. The adjusted analysis for Model 6 found a marginally significant negative association between direct bilirubin and current dioxin when occupation and the current dioxin-by-lifetime alcohol history interaction were removed from the final model (Table I-3-13(b): $p=0.065$).

LDH (Continuous)

The unadjusted Model 1 analysis did not show a significant group difference in the mean levels of LDH (Table 13-23(a): $p>0.13$ for all contrasts). The group-by-age and group-by-lifetime alcohol history interactions were significant in the adjusted analysis of Model 1 (Table 13-23(b): $p=0.002$ and $p=0.011$ respectively). Appendix Table I-2-14

Table 13-23.
Analysis of LDH (U/L)
(Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	*Ranch Hand*	*938*	*145.69*	*0.24 --*	*0.826*
	Comparison	*1,252*	*145.45*		
Officer	Ranch Hand	360	144.21	-0.53 --	0.759
	Comparison	495	144.73		
Enlisted Flyer	Ranch Hand	162	143.45	-4.10 --	0.133
	Comparison	196	147.55		
Enlisted Groundcrew	Ranch Hand	416	147.89	2.53 --	0.137
	Comparison	561	145.36		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED						
Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]	Covariate Remarks[d]
All	*Ranch Hand*	*916*	*145.33***	*0.36 --***	*0.743***	GROUP*AGE (p=0.002)
	Comparison	*1,231*	*144.97***			GROUP*DRKYR (p=0.011)
Officer	Ranch Hand	356	143.05**	-0.49 --**	0.779**	OCC (p=0.016)
	Comparison	487	143.55**			ALC*DRKYR (p=0.007)
Enlisted Flyer	Ranch Hand	156	142.49**	-4.03 --**	0.139**	ALC*DC (p=0.022)
	Comparison	195	146.51**			
Enlisted Groundcrew	Ranch Hand	404	148.97**	2.81 --**	0.096**	
	Comparison	549	146.15**			

[a] Transformed from natural logarithm scale.

[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

[c] P-values based on difference of means on natural logarithm scale.

[d] Covariates and associated p-values correspond to final model based on all participants with available data.

** Group-by-covariate interactions ($p \leq 0.05$); adjusted mean, difference of adjusted means, confidence interval, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table I-2-14 for further analysis of these interactions.

Table 13-23. (Continued)
Analysis of LDH (U/L)
(Continuous)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	173	146.72	146.95	0.007	0.0020 (0.0058)	0.735
Medium	170	143.15	143.23			
High	172	148.46	148.15			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[d]			
Initial Dioxin	n	Adj. Mean[ad]	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
Low	171	146.10	0.032	-0.0012 (0.0067)	0.863	OCC (p=0.070) RACE*ALC (p=0.025)
Medium	167	142.24				
High	170	145.89				

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Slope and standard error based on natural logarithm of LDH versus $\log_2$ (initial dioxin).

[d] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 13-23. (Continued)
Analysis of LDH (U/L)
(Continuous)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED					
Dioxin Category	**n**	**Mean[a]**	**Adj. Mean[ab]**	**Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]**	**p-Value[d]**
Comparison	1,042	145.91	145.87		
Background RH	369	144.66	145.56	-0.31 --	0.843
Low RH	257	146.39	146.09	0.22 --	0.904
High RH	258	145.82	144.96	-0.91 --	0.612
Low plus High RH	515	146.11	145.53	-0.35 --	0.803

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED					
Dioxin Category	**n**	**Adj. Mean[ae]**	**Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]**	**p-Value[d]**	**Covariate Remarks**
Comparison	1,024	147.47**			DXCAT*AGE (p=0.003) DXCAT*RACE (p=0.028) DXCAT*DRKYR (p=0.040) OCC (p=0.001)
Background RH	362	147.90**	0.43 --**	0.793**	
Low RH	251	147.40**	-0.07 --**	0.971**	
High RH	251	146.55**	-0.92 --**	0.625**	
Low plus High RH	502	146.98**	-0.50 --**	0.729**	

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not presented because analysis was performed on natural logarithm scale.

[d] P-value is based on difference of means on natural logarithm scale.

[e] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interactions ($p \leq 0.05$); adjusted mean, difference of adjusted means, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table I-2-14 for further analysis of these interactions.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 13-23. (Continued)
Analysis of LDH (U/L)
(Continuous)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED						
	Current Dioxin Category Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)		
Model[b]	Low	Medium	High	R^2	Slope (Std. Error)[c]	p-Value
4	144.01 (290)	147.09 (298)	145.38 (296)	0.002	0.0049 (0.0039)	0.211
5	143.82 (294)	146.63 (297)	146.07 (293)	0.002	0.0042 (0.0033)	0.208
6[d]	144.06 (293)	146.65 (297)	145.83 (293)	0.002	0.0034 (0.0036)	0.341

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED							
	Current Dioxin Category Adjusted Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)			
Model[b]	Low	Medium	High	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
4	143.83 (289)	146.50 (295)	143.14 (291)	0.020	0.0020 (0.0045)	0.654	OCC (p=0.024) ALC*DC (p=0.020)
5	143.51 (292)	145.78 (295)	144.13 (288)	0.020	0.0017 (0.0038)	0.660	OCC (p=0.022) ALC*DC (p=0.020)
6[e]	143.76 (291)	145.82 (295)	143.90 (288)	0.020	0.0009 (0.0041)	0.820	OCC (p=0.022) ALC*DC (p=0.021)

[a] Transformed from natural logarithm scale.

[b] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[c] Slope and standard error based on natural logarithm of LDH versus log_2 (current dioxin + 1).

[d] Adjusted for log_2 total lipids.

[e] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

presents adjusted results stratified separately by age and lifetime alcohol history. In addition, the adjusted analysis contained occupation and two covariate-by-covariate interactions: current alcohol use-by-lifetime alcohol history, and current alcohol use-by-degreasing chemical exposure. The adjusted analysis did not show a significant overall group difference when the two group-by-covariate interactions were removed from the final model (Table 13-23(b): $\bar{p}=0.743$). However, the stratified adjusted analysis detected a marginally significant group difference within the enlisted groundcrew stratum (Table 13-23(b): $p=0.096$). For the enlisted groundcrew, the adjusted mean level of LDH was higher for the Ranch Hands than for the Comparisons (148.97 U/L vs. 146.15 U/L).

The unadjusted and adjusted Model 2 analyses did not show a significant association between lactic dehydrogenase and initial dioxin (Table 13-23(c,d): $p>0.73$ for both analyses). The final adjusted model contained occupation and the race-by-current alcohol use interaction.

For Model 3, the unadjusted analysis did not reveal any of the Ranch Hand categories to be significantly different from the Comparison group (Table 13-23(e): $p>0.61$ for all contrasts). Categorized dioxin-by-age, categorized dioxin-by-race, and categorized dioxin-by-lifetime alcohol history were significant interactions in the adjusted analysis of Model 3 (Table 13-23(f): $p=0.003$, $p=0.028$, and $p=0.040$ respectively). Appendix Table I-2-14 presents adjusted results stratified separately by age, race, and lifetime alcohol history. The adjusted analysis also included occupation. Without the three categorized dioxin-by-covariate interactions, the adjusted analysis did not show a significant contrast with the Comparison group (Table 13-23(f): $p>0.62$ for all contrasts).

The unadjusted and adjusted results for Models 4 through 6 did not reveal a significant association between LDH and current dioxin (Table 13-23(g,h): $p>0.20$ for all analyses). Each of the final adjusted models contained occupation and the current alcohol use-by-degreasing chemical exposure interaction.

LDH (Discrete)

The unadjusted Model 1 analysis did not reveal a significant group difference in the percentage of LDH abnormalities (Table 13-24(a): $p>0.80$ for all contrasts). The adjusted analysis contained a significant interaction between group and current alcohol use (Table 13-24(b): $p=0.015$). The final adjusted model contained age, race, and two significant interactions: degreasing chemical exposure-by-occupation and degreasing chemical exposure-by-lifetime alcohol history. Appendix Table I-2-15 displays adjusted results stratified by current alcohol use. When the group-by-current alcohol use interaction was removed from the final model, the adjusted analysis did not detect a significant group difference (Table 13-24(b): $p>0.58$ for all contrasts).

For Model 2, the unadjusted and adjusted results did not reveal a significant association between LDH and initial dioxin (Table 13-24(c,d): $p>0.22$ for both analyses). Current alcohol use was the only covariate retained in the adjusted analysis.

Table 13-24.
Analysis of LDH
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent High**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	*Ranch Hand*	*938*	*14.4*	*1.01 (0.80,1.29)*	*0.957*
	Comparison	*1,252*	*14.2*		
Officer	Ranch Hand	360	13.1	0.98 (0.65,1.46)	0.987
	Comparison	495	13.3		
Enlisted Flyer	Ranch Hand	162	14.8	0.96 (0.54,1.72)	0.999
	Comparison	196	15.3		
Enlisted Groundcrew	Ranch Hand	416	15.4	1.06 (0.74,1.51)	0.809
	Comparison	561	14.6		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	*1.05 (0.82,1.34)***	*0.696***	GROUP*ALC (p=0.015)
Officer	1.01 (0.67,1.52)**	0.976**	AGE (p=0.013) RACE (p=0.046)
Enlisted Flyer	1.00 (0.55,1.82)**	0.999**	DC*OCC (p=0.038)
Enlisted Groundcrew	1.11 (0.77,1.59)**	0.585**	DC*DRKYR (p=0.021)

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

** Group-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-15 for further analysis of this interaction.

Table 13-24. (Continued)
Analysis of LDH
(Discrete)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	173	12.1	1.10 (0.92,1.32)	0.302
Medium	170	13.5		
High	172	16.3		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
508	1.12 (0.93,1.35)	0.222	ALC (p=0.004)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 13-24. (Continued)
Analysis of LDH
(Discrete)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	**n**	**Percent High**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,042	14.4		
Background RH	369	13.3	1.01 (0.71,1.44)	0.945
Low RH	257	12.5	0.82 (0.54,1.23)	0.332
High RH	258	15.5	0.99 (0.68,1.46)	0.977
Low plus High RH	515	14.0	0.91 (0.67,1.23)	0.525

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	**n**	**Adj. Relative Risk (95% C.I.)[ac]**	**p-Value**	**Covariate Remarks**
Comparison	1,024			DXCAT*DRKYR (p=0.004)
				RACE (p=0.006)
Background RH	362	1.12 (0.77,1.62)**	0.549**	AGE (p=0.075)
				ALC (p=0.002)
Low RH	251	0.83 (0.54,1.26)**	0.383**	OCC*DC (p=0.032)
High RH	251	1.05 (0.70,1.57)**	0.801**	
Low plus High RH	502	0.94 (0.68,1.29)**	0.689**	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interaction ($p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-15 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 13-24. (Continued)
Analysis of LDH
(Discrete)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent High/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	13.8 (290)	13.1 (298)	14.2 (296)	1.07 (0.94,1.21)	0.340
5	12.9 (294)	12.8 (297)	15.4 (293)	1.06 (0.95,1.19)	0.312
6[c]	13.0 (293)	12.8 (297)	15.4 (293)	1.04 (0.92,1.17)	0.561

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	875	1.08 (0.94,1.23)	0.278	ALC (p=0.001)
5	875	1.07 (0.95,1.20)	0.277	ALC (p=0.001)
6[d]	874	1.05 (0.93,1.19)	0.461	ALC (p=0.001)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

The unadjusted analysis for Model 3 did not reveal a significant contrast between any of the Ranch Hand categories and the Comparison group (Table 13-24(e): $p>0.33$ for all contrasts). Categorized dioxin-by-lifetime alcohol history was a significant interaction in the adjusted Model 3 analysis (Table 13-24(f): $p=0.004$). Also included in the adjusted analysis were race, age, current alcohol use, and the occupation-by-degreasing chemical exposure interaction. Appendix Table I-2-15 shows adjusted results stratified by lifetime alcohol history. After removing the categorized dioxin-by-lifetime alcohol history interaction from the final model, the adjusted analysis did not reveal any of the Ranch Hand categories to be significantly different from the Comparison group (Table 13-24(f): $p>0.38$ for all contrasts).

The unadjusted and adjusted analyses for Models 4 through 6 did not show a significant association between LDH and current dioxin (Table 13-24(g,h): $p>0.27$ for all analyses). Current alcohol use was the only covariate retained in each of the adjusted analyses.

Cholesterol (Continuous)

The unadjusted Model 1 analysis did not reveal a significant group difference in the mean levels of cholesterol (Table 13-25(a): $p>0.36$ for all contrasts). The interaction between group and current alcohol use was significant in the adjusted Model 1 analysis (Table 13-25(b): $p=0.035$). The adjusted model also contained occupation, degreasing chemical exposure, and the age-by-lifetime alcohol history interaction. Appendix Table I-2-16 displays adjusted results stratified by current alcohol use. The adjusted analysis did not reveal a significant group contrast when the group-by-current alcohol use interaction was removed from the final model (Table 13-25(b): $p>0.36$ for all contrasts).

The unadjusted Model 2 results did not reveal a significant association between cholesterol and initial dioxin (Table 13-25(c): $p=0.215$). The adjusted analysis for Model 2 contained a significant interaction between initial dioxin and degreasing chemical exposure (Table 13-25(d): $p=0.023$). Appendix Table I-2-16 shows adjusted results stratified by degreasing chemical exposure. Age and current alcohol use also were significant covariates in the adjusted analysis. In contrast to the unadjusted analysis, the adjusted analysis detected a marginally significant positive association between cholesterol and initial dioxin when the initial dioxin-by-degreasing chemical exposure interaction was removed from the final model (Table 13-25(d): $p=0.080$, Adj. Slope=0.0113).

For Model 3, the unadjusted analysis of cholesterol did not reveal any of the Ranch Hand categories to be significantly different from the Comparison group (Table 13-25(e): $p>0.15$ for all contrasts). The adjusted Model 3 analysis contained a significant interaction between categorized dioxin and lifetime alcohol history (Table 13-25(f): $p=0.047$). Appendix Table I-2-16 displays adjusted results stratified by lifetime alcohol history. The final adjusted model also contained four covariate-by-covariate interactions: age-by-lifetime alcohol history, race-by-occupation, occupation-by-lifetime alcohol history, and current alcohol use-by-degreasing chemical exposure. After removing the categorized dioxin-by-lifetime alcohol history interaction from the final model, the adjusted analysis did not show a significant difference between any of the Ranch Hand categories and the Comparison group (Table 13-25(f): $p>0.38$ for all contrasts).

Table 13-25.
Analysis of Cholesterol (mg/dl)
(Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Mean[a]**	**Difference of Means (95% C.I.)[b]**	**p-Value[c]**
All	*Ranch Hand*	*939*	*215.57*	*0.64 --*	*0.703*
	Comparison	*1,253*	*214.93*		
Officer	Ranch Hand	361	214.16	2.30 --	0.365
	Comparison	495	211.86		
Enlisted Flyer	Ranch Hand	162	219.24	-2.88 --	0.495
	Comparison	196	222.12		
Enlisted Groundcrew	Ranch Hand	416	215.38	0.19 --	0.942
	Comparison	562	215.19		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED						
Occupational Category	**Group**	**n**	**Adj. Mean[a]**	**Difference of Adj. Means (95% C.I.)[b]**	**p-Value[c]**	**Covariate Remarks[d]**
All	*Ranch Hand*	*917*	*216.07***	*0.58 --***	*0.729***	GROUP*ALC (p=0.035)
	Comparison	*1,232*	*215.49***			OCC (p=0.011)
						DC (p=0.137)
Officer	Ranch Hand	357	213.61**	2.41 --**	0.365**	AGE*DRKYR (p=0.030)
	Comparison	487	211.20**			
Enlisted Flyer	Ranch Hand	156	217.80**	-3.04 --**	0.473**	
	Comparison	195	220.84**			
Enlisted Groundcrew	Ranch Hand	404	215.66**	0.26 --**	0.918**	
	Comparison	550	215.40**			

[a] Transformed from natural logarithm scale.

[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

[c] P-values based on difference of means on natural logarithm scale.

[d] Covariates and associated p-values correspond to final model based on all participants with available data.

** Group-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted mean, difference of adjusted means, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-16 for further analysis of this interaction.

Table 13-25. (Continued)
Analysis of Cholesterol (mg/dl)
(Continuous)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	173	216.17	216.05	0.004	0.0076 (0.0061)	0.215
Medium	170	214.25	214.16			
High	172	218.20	218.42			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[d]			
Initial Dioxin	n	Adj. Mean[ad]	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
Low	171	214.68**	0.033	0.0113 (0.0064)**	0.080**	INIT*DC (p=0.023) AGE (p=0.031) ALC (p=0.019)
Medium	167	213.07**				
High	170	218.87**				

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Slope and standard error based on natural logarithm of cholesterol versus $\log_2$ (initial dioxin).

[d] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-16 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 13-25. (Continued)
Analysis of Cholesterol (mg/dl)
(Continuous)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED					
Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,043	214.44	214.44		
Background RH	369	214.41	214.04	-0.40 --	0.864
Low RH	257	214.37	214.77	0.33 --	0.901
High RH	258	218.06	218.20	3.76 --	0.159
Low plus High RH	515	216.21	216.48	2.04 --	0.323

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED					
Dioxin Category	n	Adj. Mean[ae]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]	Covariate Remarks
Comparison	1,025	218.97**			DXCAT*DRKYR (p=0.047)
					AGE*DRKYR (p=0.042)
Background RH	362	219.72**	0.75 --**	0.757**	RACE*OCC (p=0.035)
					OCC*DRKYR (p=0.042)
Low RH	251	218.49**	-0.48 --**	0.861**	ALC*DC (p=0.032)
High RH	251	221.45**	2.48 --**	0.381**	
Low plus High RH	502	219.96**	1.00 --**	0.641**	

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not presented because analysis was performed on natural logarithm scale.

[d] P-value is based on difference of means on natural logarithm scale.

[e] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interaction ($0.01<p\leq0.05$); adjusted mean, difference of adjusted means, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-16 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 13-25. (Continued)
Analysis of Cholesterol (mg/dl)
(Continuous)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED						
	Current Dioxin Category Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)		
Model[b]	Low	Medium	High	R^2	Slope (Std. Error)[c]	p-Value
4	214.75 (290)	214.34 (298)	217.29 (296)	0.002	0.0058 (0.0041)	0.162
5	210.19 (294)	215.71 (297)	220.61 (293)	0.019	0.0145 (0.0035)	<0.001
6[d]	218.50 (293)	216.53 (297)	211.37 (293)	0.272	-0.0054 (0.0033)	0.098

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED							
	Current Dioxin Category Adjusted Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)			
Model[b]	Low	Medium	High	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
4	214.88 (287)	213.93 (290)	217.37 (287)	0.041	0.0066 (0.0043)	0.129	ALC (p<0.001) AGE*DRKYR (p=0.009) AGE*DC (p=0.013)
5	210.42 (290)	215.33 (290)	221.28 (284)	0.059	0.0155 (0.0036)	<0.001	ALC (p<0.001) AGE*DRKYR (p=0.007) AGE*DC (p=0.012)
6[e]	218.83 (289)	216.64 (290)	211.45 (284)	0.294	-0.0055 (0.0036)	0.129	ALC (p<0.001) AGE*DRKYR (p=0.008) AGE*DC (p=0.004)

[a] Transformed from natural logarithm scale.

[b] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[c] Slope and standard error based on natural logarithm of cholesterol versus log_2 (current dioxin + 1).

[d] Adjusted for log_2 total lipids.

[e] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

The unadjusted Model 4 analysis did not reveal a significant association between cholesterol and current dioxin (Table 13-25(g): $p=0.162$), but a significant and a marginally significant association was detected in the unadjusted analyses of Models 5 and 6 respectively (Table 13-25(g): $p<0.001$, Est. Slope=0.0145 and $p=0.098$, Est. Slope=-0.0054). Also, the estimated slopes for Models 5 and 6 differed in sign.

The adjusted results for Models 4 through 6 differed from the unadjusted results. After covariate adjustment, the analyses of Models 4 and 6 did not show a significant association between cholesterol and current dioxin (Table 13-25(h): $p=0.129$ for both analyses). However, the adjusted Model 5 analysis did show a significant association (Table 13-25(h): $p<0.001$, Adj. Slope=0.0155). Each of the adjusted analyses contained current alcohol use and two covariate-by-covariate interactions: age-by-lifetime alcohol history and age-by-degreasing chemical exposure.

Cholesterol (Discrete)

The unadjusted Model 1 analysis did not show a significant group difference in the percentage of individuals with high cholesterol (Table 13-26(a): $p>0.21$ for all contrasts). The adjusted Model 1 analysis contained a significant group-by-current alcohol use interaction (Table 13-26(b): $p=0.001$). In addition to this interaction, the final model contained occupation and an interaction between race and industrial chemical exposure. Appendix Table I-2-17 displays adjusted results stratified by current alcohol use. When the group-by-current alcohol use interaction was removed from the final model, the adjusted analysis did not reveal a significant group contrast (Table 13-26(b): $p>0.10$ for all contrasts).

For Model 2, the unadjusted analysis did not show a significant association between cholesterol and initial dioxin (Table 13-26(c): $p=0.926$).

Initial dioxin-by-degreasing chemical exposure and initial dioxin-by-lifetime alcohol history were significant interactions in the adjusted Model 2 analysis (Table 13-26(d): $p=0.018$ and $p=0.014$ respectively). Appendix Table I-2-17 presents adjusted results stratified separately by degreasing chemical exposure and lifetime alcohol history. The final adjusted model contained age and the interaction between race and current alcohol use. The adjusted analysis did not reveal a significant association between cholesterol and initial dioxin when the two initial dioxin-by-covariate interactions were removed from the final model ($p=0.480$).

The unadjusted Model 3 results revealed a marginally significant difference between the low plus high Ranch Hands and the Comparisons in the percentage of individuals with high cholesterol (Table 13-16(e): $p=0.091$, Est. RR=1.30, 95% C.I.=[0.96, 1.75]). The percentage of participants with high cholesterol was greater for the low plus high Ranch Hands than for the Comparison group (15.7% vs. 12.7%).

The adjusted Model 3 analysis contained a significant interaction between categorized dioxin and current alcohol use (Table 13-26(f): $p=0.014$). Appendix Table I-2-17 displays adjusted results stratified by current alcohol use. Besides the categorized dioxin-by-current

Table 13-26.
Analysis of Cholesterol
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent High**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	*Ranch Hand*	*939*	*15.0*	*1.13 (0.89,1.44)*	*0.340*
	Comparison	*1,253*	*13.5*		
Officer	Ranch Hand	361	12.2	1.13 (0.74,1.73)	0.637
	Comparison	495	10.9		
Enlisted Flyer	Ranch Hand	162	19.8	1.48 (0.85,2.58)	0.216
	Comparison	196	14.3		
Enlisted Groundcrew	Ranch Hand	416	15.6	1.01 (0.71,1.43)	0.999
	Comparison	562	15.5		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	*1.15 (0.90,1.47)***	*0.252***	GROUP*ALC (p<0.001) OCC (p=0.015) RACE*IC (p=0.007)
Officer	1.14 (0.74,1.74)**	0.557**	
Enlisted Flyer	1.60 (0.91,2.80)**	0.101**	
Enlisted Groundcrew	1.03 (0.72,1.46)**	0.889**	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

** Group-by-covariate interaction ($p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-17 for further analysis of this interaction.

Table 13-26. (Continued)
Analysis of Cholesterol
(Discrete)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	173	16.2	1.01 (0.84,1.21)	0.926
Medium	170	14.7		
High	172	16.3		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
502	1.07 (0.88,1.31)**	0.480**	INIT*DC (p=0.018) INIT*DRKYR (p=0.014) AGE (p=0.079) RACE*ALC (p=0.024)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interactions ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table I-2-17 for further analyses of these interactions.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 13-26. (Continued)
Analysis of Cholesterol
(Discrete)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	**n**	**Percent High**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,043	12.7		
Background RH	369	13.6	1.07 (0.75,1.53)	0.697
Low RH	257	14.8	1.22 (0.83,1.81)	0.313
High RH	258	16.7	1.37 (0.94,2.00)	0.101
Low plus High RH	515	15.7	1.30 (0.96,1.75)	0.091

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	**n**	**Adj. Relative Risk (95% C.I.)[ac]**	**p-Value**	**Covariate Remarks**
Comparison	1,027			DXCAT*ALC (p=0.014) AGE (p=0.044) OCC (p=0.003) RACE*IC (p=0.016)
Background RH	367	1.22 (0.84,1.76)**	0.294**	
Low RH	254	1.24 (0.84,1.84)**	0.285**	
High RH	254	1.25 (0.84,1.84)**	0.271**	
Low plus High RH	508	1.24 (0.91,1.69)**	0.165**	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-17 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 13-26. (Continued)
Analysis of Cholesterol
(Discrete)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent High/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	13.8 (290)	14.8 (298)	15.9 (296)	1.06 (0.94,1.21)	0.332
5	11.2 (294)	14.8 (297)	18.4 (293)	1.18 (1.06,1.32)	0.003
6[c]	11.3 (293)	14.8 (297)	18.4 (293)	0.94 (0.83,1.07)	0.360

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	864	1.02 (0.88,1.19)	0.781	AGE (p=0.105) OCC (p=0.086) DRKYR (p=0.072) RACE*ALC (p=0.019)
5	864	1.18 (1.03,1.36)**	0.002**	CURR*OCC (p=0.025) DRKYR (p=0.075) RACE*ALC (p=0.016) DC*AGE (p=0.026)
6[d]	863	0.95 (0.82,1.09)	0.431	ALC (p<0.001) DRKYR (p=0.149) DC*AGE (p=0.024)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-17 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

alcohol use interaction, the final model also included occupation, age, and the race-by-industrial chemical exposure interaction. In contrast to the unadjusted results, the adjusted analysis did not show any of the Ranch Hand categories to be significantly different from the Comparison group (Table 13-26(f): $p>0.16$ for all contrasts).

Removing occupation from the final model affected the adjusted results. Without occupation and the categorized dioxin-by-current alcohol use interaction, the adjusted analysis detected marginally significant relative risks for the high Ranch Hands and low plus high Ranch Hands (Appendix Table I-3-17(a): $p=0.073$, Adj. RR=1.42, 95% C.I.=[0.97, 2.10] and $p=0.067$, Adj. RR=1.33, 95% C.I.=[0.98, 1.81] respectively).

The unadjusted analyses for Models 4 and 6 did not show a significant association between cholesterol and current dioxin (Table 13-26(g): $p>0.33$ for both analyses). However, the unadjusted Model 5 analysis showed a significant positive association between cholesterol and current dioxin (Table 13-26(g): $p=0.003$, Est. RR=1.18, 95% C.I.=[1.06, 1.32]).

Similar to the unadjusted results, the adjusted analyses for Models 4 and 6 did not show a significant association between cholesterol and current dioxin (Table 13-26(h): $p>0.43$ for both analyses). For Model 4, the final model contained age, occupation, lifetime alcohol history, and the race-by-current alcohol use interaction. Model 6 contained current alcohol use, lifetime alcohol history, and the degreasing chemical exposure-by-age interaction.

The adjusted analysis for Model 5 contained a significant interaction between current dioxin and occupation (Table 13-26(h): $p=0.025$). Appendix Table I-2-17 presents adjusted results for Model 5 stratified by occupation. The adjusted Model 5 analysis also included lifetime alcohol history and two covariate-by-covariate interactions, race-by-current alcohol use and degreasing chemical exposure-by-age. When the current dioxin-by-occupation interaction was removed from the final model, the adjusted analysis detected a significant positive association between cholesterol and current dioxin (Table 13-26(h): $p=0.002$, Adj. RR=1.18, 95% C.I.=[1.03, 1.36]).

HDL Cholesterol (Continuous)

The unadjusted Model 1 analysis did not reveal a significant group difference in the mean levels of HDL cholesterol (Table 13-27(a): $p>0.24$ for all contrasts). The adjusted analysis for Model 1 contained two significant group-by-covariate interactions: group-by-current alcohol use and group-by-lifetime alcohol history (Table 13-27(b): $p<0.001$ and $p=0.023$ respectively). Appendix Table I-2-18 presents adjusted results stratified separately by current alcohol use and lifetime alcohol history. The final model also contained occupation and five covariate-by-covariate interactions: age-by-degreasing chemical exposure, race-by-industrial chemical exposure, race-by-degreasing chemical exposure, lifetime alcohol history-by-current alcohol use, and current alcohol use-by-industrial chemical exposure. The adjusted analysis did not reveal a significant group contrast after the two group-by-covariate interactions were removed from the final model (Table 13-27(b): $p>0.33$).

Table 13-27.
Analysis of HDL Cholesterol (mg/dl)
(Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Mean[a]**	**Difference of Means (95% C.I.)[b]**	**p-Value[c]**
All	***Ranch Hand***	***925***	***40.56***	***-0.36 --***	***0.429***
	Comparison	***1,241***	***40.91***		
Officer	Ranch Hand	353	42.15	-0.08 --	0.918
	Comparison	491	42.23		
Enlisted Flyer	Ranch Hand	158	40.38	0.29 --	0.785
	Comparison	193	40.09		
Enlisted Groundcrew	Ranch Hand	414	39.31	-0.76 --	0.244
	Comparison	557	40.07		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED						
Occupational Category	**Group**	**n**	**Adj. Mean[a]**	**Difference of Adj. Means (95% C.I.)[b]**	**p-Value[c]**	**Covariate Remarks[d]**
All	***Ranch Hand***	***903***	***42.61*****	***-0.20 --*****	***0.656*****	GROUP*ALC (p<0.001)
	Comparison	***1,221***	***42.81*****			GROUP*DRKYR (p=0.023)
Officer	Ranch Hand	349	44.29**	-0.27 --**	0.727**	OCC (p<0.001)
	Comparison	484	44.56**			AGE*DC (p=0.026)
						RACE*IC (p=0.010)
Enlisted Flyer	Ranch Hand	152	42.55**	1.08 --**	0.335**	RACE*DC (p=0.024)
	Comparison	192	41.47**			DRKYR*ALC (p=0.025)
Enlisted Groundcrew	Ranch Hand	402	41.49**	-0.62 --**	0.356**	ALC*IC (p=0.042)
	Comparison	545	42.11**			

[a] Transformed from natural logarithm scale.

[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

[c] P-values based on difference of means on natural logarithm scale.

[d] Covariates and associated p-values correspond to final model based on all participants with available data.

** Group-by-covariate interactions ($p \leq 0.05$); adjusted mean, difference of adjusted means, confidence interval, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table I-2-18 for further analysis of these interactions.

Table 13-27. (Continued)
Analysis of HDL Cholesterol (mg/dl)
(Continuous)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	172	41.12	40.91	0.045	-0.0176 (0.0083)	0.035
Medium	166	38.69	38.64			
High	168	38.88	39.15			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[d]			
Initial Dioxin	n	Adj. Mean[ad]	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
Low	170	41.56	0.195	-0.0052 (0.0090)	0.563	OCC (p=0.073) RACE*IC (p=0.025) ALC*DC (p=0.009)
Medium	163	40.20				
High	166	41.17				

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Slope and standard error based on natural logarithm of HDL cholesterol versus $\log_2$ (initial dioxin).

[d] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 13-27. (Continued)
Analysis of HDL Cholesterol (mg/dl)
(Continuous)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,033	40.74	40.78		
Background RH	365	42.23	41.49	0.72 --	0.247
Low RH	253	40.66	40.89	0.11 --	0.872
High RH	253	38.51	39.13	-1.65 --	0.017
Low plus High RH	506	39.57	40.00	-0.78 --	0.150

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Mean[ae]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]	Covariate Remarks
Comparison	1,016	42.57**			DXCAT*ALC ($p<0.001$) DXCAT*DRKYR ($p=0.008$) RACE ($p<0.001$) OCC ($p<0.001$) ALC*IC ($p=0.044$)
Background RH	358	43.01**	0.44 --**	0.495**	
Low RH	247	42.60**	0.03 --**	0.967**	
High RH	246	41.72**	-0.85 --**	0.250**	
Low plus High RH	493	42.16**	-0.41 --**	0.463**	

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not presented because analysis was performed on natural logarithm scale.

[d] P-value is based on difference of means on natural logarithm scale.

[e] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interactions ($p \leq 0.05$); adjusted mean, difference of adjusted means, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table I-2-18 for further analysis of these interactions.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 13-27. (Continued)
Analysis of HDL Cholesterol (mg/dl)
(Continuous)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED						
	Current Dioxin Category Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)		
Model[b]	Low	Medium	High	R^2	Slope (Std. Error)[c]	p-Value
4	42.62 (288)	40.95 (293)	38.52 (290)	0.022	-0.0269 (0.0061)	<0.001
5	42.95 (294)	40.79 (294)	38.28 (283)	0.027	-0.0255 (0.0052)	<0.001
6[d]	42.41 (293)	40.75 (294)	38.82 (283)	0.041	-0.0187 (0.0055)	0.001

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED							
	Current Dioxin Category Adjusted Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)			
Model[b]	Low	Medium	High	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
4	44.30** (285)	42.59** (285)	40.72** (281)	0.131	-0.0218 (0.0067)**	0.001**	CURR*DRKYR (p=0.007) CURR*ALC (p=0.033) RACE (p=0.033) AGE*DC (p=0.028) OCC*ALC (p=0.042)
5	44.77** (290)	42.34** (287)	40.36** (274)	0.141	-0.0225 (0.0057)**	<0.001**	CURR*DRKYR (p=0.001) CURR*ALC (p=0.020) RACE (p=0.040) AGE*DC (p=0.032) OCC*ALC (p=0.042)
6[e]	43.80** (289)	42.02** (287)	40.87** (274)	0.165	-0.0138 (0.0060)**	0.022**	CURR*DRKYR (p=0.002) CURR*ALC (p=0.030) CURR*DC (p=0.048) RACE (p=0.082) AGE*DC (p=0.017) OCC*ALC (p=0.046)

[a] Transformed from natural logarithm scale.

[b] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[c] Slope and standard error based on natural logarithm of HDL cholesterol versus log_2 (current dioxin + 1).

[d] Adjusted for log_2 total lipids.

[e] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($p \leq 0.05$); adjusted mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-18 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

The unadjusted Model 2 results revealed a significant inverse association between HDL cholesterol and initial dioxin (Table 13-27(c): $p=0.035$, Est. Slope=-0.0176). In contrast to the unadjusted analysis, the adjusted analysis did not reveal a significant association between HDL cholesterol and initial dioxin (Table 13-27(d): $p=0.563$). The final model contained occupation and two interactions: race-by-industrial chemical exposure and current alcohol use-by-degreasing chemical exposure. When occupation was removed from the final model, the association between HDL cholesterol and initial dioxin became marginally significant (Appendix Table I-3-18: $p=0.066$).

The unadjusted Model 3 analysis detected a significant difference in the mean levels of HDL cholesterol between the high Ranch Hands and Comparisons (Table 13-27(e): $p=0.017$). The mean level of HDL cholesterol, adjusted for percent body fat at the time of duty in SEA and the change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, was lower for the high Ranch Hand category than for the Comparison group (39.13 mg/dl vs. 40.78 mg/dl). The categorized dioxin-by-current alcohol use and categorized dioxin-by-lifetime alcohol history interactions were significant in the adjusted analysis. Appendix Table I-2-18 presents adjusted results stratified separately by current alcohol use and lifetime alcohol history. Without the two categorized dioxin-by-covariate interactions, the adjusted Model 3 analysis did not show any of the Ranch Hand categories to be significantly different from the Comparison group (Table 13-27(f): $p \geq 0.25$ for all contrasts).

Removing occupation from the adjusted analysis affected the significance level of the contrast between the high Ranch and comparisons. Without occupation and the two categorized dioxin-by-covariate interactions, the adjusted analysis found a significant difference between the high Ranch Hands and Comparisons (Appendix Table I-3-18(b): $p=0.027$).

Each of the unadjusted analyses for Models 4 through 6 detected a significant inverse association between HDL cholesterol and current dioxin (Table 13-27(g): $p<0.001$, Est. Slope=-0.0269; $p<0.001$, Est. Slope=-0.0255; and $p=0.001$, Est. Slope=-0.0187 for Models 4, 5, and 6 respectively).

Current dioxin-by-lifetime alcohol history and current dioxin-by-current alcohol interactions were significant in the adjusted analyses of Models 4 through 6 (Table 13-27(h): $p=0.007$, $p=0.033$; $p=0.001$, $p=0.020$; and $p=0.002$, $p=0.030$ for Models 4, 5, and 6 respectively). The adjusted analysis for Model 6 also contained a significant interaction between current dioxin and degreasing chemical exposure (Table 13-27(h): $p=0.048$). Appendix Table I-2-18 presents adjusted results stratified separately by lifetime alcohol history and current alcohol use for Models 4 through 6, as well as adjusted results for Model 6 stratified by degreasing chemical exposure. Each of the adjusted analyses for Models 4 through 6 revealed a significant inverse association between HDL cholesterol and current dioxin when all of the current dioxin-by-covariate interactions were removed from the models (Table 13-27(h): $p=0.001$, Adj. Slope=-0.0218; $p<0.001$, Adj. Slope=-0.0225; and $p=0.022$, Adj. Slope=-0.0138 for Models 4, 5, and 6 respectively).

HDL Cholesterol (Discrete)

The unadjusted Model 1 analysis detected a marginally significant overall group difference in the percentage of individuals with low levels of HDL cholesterol (Table 13-28(a): $p=0.064$, Est. RR=1.33, 95% C.I.=[0.99, 1.77]). Ranch Hands were more likely than Comparisons to have low levels of HDL cholesterol (10.9% vs. 8.5%). Stratifying the analysis by occupation revealed a marginally significant group difference for the officers (Table 13-28(a): $p=0.077$, Est. RR=1.57, 95% C.I.=[0.98, 2.51]). Within the officer stratum, the percentage of HDL cholesterol abnormalities was higher for the Ranch Hands than for the Comparisons (11.3% vs. 7.5%).

After adjusting for the race-by-current alcohol use and occupation-by-current alcohol use interactions, both marginally significant contrasts in the unadjusted analysis became significant (Table 13-28(b): $p=0.048$, Adj. RR=1.34, 95% C.I.=[1.00, 1.79] and $p=0.048$, Adj. RR=1.61, 95% C.I.=[1.00, 2.59]) for the overall group contrast and the officer group contrast respectively).

The unadjusted and adjusted Model 2 results did not show a significant association between HDL cholesterol and initial dioxin (Table 13-28(c,d): $p>0.51$ for both analyses). Race and current alcohol use were the only significant terms in the adjusted model.

The unadjusted Model 3 analysis revealed a marginally significant difference in HDL cholesterol abnormalities between the background Ranch Hands and Comparison group (Table 13-28(e): $p=0.061$, Est. RR=1.48, 95% C.I.=[0.98, 2.23]). The percentages of participants with low levels of HDL cholesterol among the background Ranch Hands and the Comparison group were 10.4 percent and 8.4 percent respectively.

The adjusted Model 3 analysis contained a significant interaction between categorized dioxin and lifetime alcohol history (Table 13-28(f): $p=0.020$). The final model also contained race and current alcohol use. Appendix Table I-2-19 presents results stratified by lifetime alcohol history. After the categorized dioxin-by-lifetime alcohol history interaction was removed from the final model, the adjusted analysis did not show any of the Ranch Hand categories to be significantly different from the Comparison group (Table 13-28(f): $p>0.10$ for all contrasts).

For Models 4 through 6, the unadjusted analyses did not reveal a significant association between low levels of HDL cholesterol and current dioxin (Table 13-28(g): $p>0.27$ for all analyses). Each of the adjusted analyses for Models 4 through 6 contained a significant interaction between current dioxin and lifetime alcohol history (Table 13-28(f): $p=0.003$, $p<0.001$, and $p<0.001$ for Models 4, 5, and 6 respectively). Appendix Table I-2-19 presents adjusted results stratified by lifetime alcohol history for each of the models. The adjusted analyses for Model 4 also included race and current alcohol use: Model 6 contained degreasing chemical exposure and current alcohol use; and Model 5 contained age, degreasing chemical exposure, and current alcohol use. The adjusted analyses for Models 4 and 6 did not reveal a significant association between HDL cholesterol and current dioxin when the current dioxin-by-lifetime alcohol history interaction was removed from both of the models (Table 13-28(h): $p>0.55$ for both analyses). However, the adjusted model 5 analysis

Table 13-28.
Analysis of HDL Cholesterol
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Low**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***925***	***10.9***	***1.33 (0.99,1.77)***	***0.064***
	Comparison	***1,241***	***8.5***		
Officer	Ranch Hand	353	11.3	1.57 (0.98,2.51)	0.077
	Comparison	491	7.5		
Enlisted Flyer	Ranch Hand	158	8.9	0.80 (0.39,1.62)	0.653
	Comparison	193	10.9		
Enlisted Groundcrew	Ranch Hand	414	11.4	1.39 (0.91,2.13)	0.159
	Comparison	557	8.4		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.34 (1.00,1.79)***	***0.048***	RACE*ALC (p=0.015) OCC*ALC (p=0.005)
Officer	1.61 (1.00,2.59)	0.048	
Enlisted Flyer	0.76 (0.37,1.56)	0.450	
Enlisted Groundcrew	1.42 (0.92,2.19)	0.110	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 13-28. (Continued)
Analysis of HDL Cholesterol
(Discrete)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Low	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	172	7.6	1.07 (0.87,1.32)	0.517
Medium	166	12.7		
High	168	11.3		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log$_2$ (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
499	1.05 (0.85,1.30)	0.638	RACE (p=0.128) ALC (p=0.012)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 13-28. (Continued)
Analysis of HDL Cholesterol
(Discrete)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Low	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,033	8.4		
Background RH	365	10.4	1.48 (0.98,2.23)	0.061
Low RH	253	8.7	0.97 (0.59,1.60)	0.913
High RH	253	12.3	1.36 (0.88,2.12)	0.169
Low plus High RH	506	10.5	1.17 (0.81,1.68)	0.405

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,016			DXCAT*DRKYR (p=0.020) RACE (p=0.041) ALC (p=0.003)
Background RH	358	1.41 (0.93,2.14)**	0.108**	
Low RH	247	1.03 (0.62,1.69)**	0.916**	
High RH	246	1.40 (0.90,2.18)**	0.141**	
Low plus High RH	493	1.21 (0.84,1.75)**	0.300**	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-19 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 13-28. (Continued)
Analysis of HDL Cholesterol
(Discrete)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Low/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	9.7 (288)	9.6 (293)	12.1 (290)	1.04 (0.90,1.20)	0.613
5	9.9 (294)	8.8 (294)	12.7 (283)	1.07 (0.94,1.22)	0.277
6[c]	9.9 (293)	8.8 (294)	12.7 (283)	0.97 (0.84,1.12)	0.676

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	851	1.05 (0.90,1.21)**	0.555**	CURR*DRKYR (p=0.003) RACE (p=0.124) ALC (p=0.015)
5	851	1.13 (0.98,1.29)**	0.085**	CURR*DRKYR (p<0.001) AGE (p=0.144) DC (p=0.140) ALC (p=0.022)
6[d]	850	1.00 (0.87,1.16)**	0.951**	CURR*DRKYR (p<0.001) DC (p=0.066) ALC (p=0.009)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-19 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

detected a marginally significant positive association after the current dioxin-by-lifetime alcohol history interaction was removed from the final model (Table 13-28(h): p=0.085, Adj. RR=1.13, 95% C.I.=[0.98, 1.29]).

Cholesterol-HDL Ratio (Continuous)

The unadjusted and adjusted Model 1 analyses of the cholesterol-HDL ratio did not reveal a significant difference between Ranch Hands and Comparisons (Table 13-29(a,b): p>0.19 for all contrasts). Race, occupation, and current alcohol use were significant in the adjusted analysis.

The unadjusted Model 2 results detected a significant positive association between cholesterol-HDL ratio and initial dioxin (Table 13-29(c): p=0.012, Est. Slope=0.0234). The adjusted Model 2 analysis contained a significant interaction between initial dioxin and current alcohol use (Table 13-29(d): p=0.006). The final model contained age and four significant covariate-by-covariate interactions: race-by-industrial chemical exposure, occupation-by-current alcohol use, lifetime alcohol history-by-industrial chemical exposure, and current alcohol use-by-degreasing chemical exposure. Appendix Table I-2-20 displays adjusted results stratified by current alcohol use. After the initial dioxin-by-current alcohol use interaction was removed from the final model, the adjusted analysis did not reveal a significant association between HDL cholesterol and initial dioxin (Table 13-29(d): p=0.178).

Removing occupation from the final model changed the statistical significance of the adjusted results. Without occupation and the initial dioxin-by-current alcohol use interaction, the adjusted Model 2 analysis detected a significant positive association between HDL cholesterol and initial dioxin (Appendix Table I-3-19(a): p=0.012, Adj. Slope=0.0243).

The unadjusted Model 3 analysis showed the mean levels of cholesterol-HDL ratio to be significantly different between the high Ranch Hand category and the Comparison group (Table 13-29(e): p=0.004). In addition, the unadjusted analysis detected a marginally significant difference between the low plus high Ranch Hand category and the Comparison group (Table 13-29(e): p=0.073). The mean levels of cholesterol-HDL ratio, adjusted for percent body fat at the time of duty in SEA and the change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, for the high and low plus high Ranch Hand categories and the Comparison group were 5.55, 5.40, and 5.25 respectively.

Categorized dioxin-by-current alcohol use was a significant interaction in the adjusted Model 3 analysis (Table 13-29(f): p=0.031). The final model also included race and occupation. Appendix Table I-2-20 displays adjusted results stratified by current alcohol use. The adjusted Model 3 analysis did not detect a significant difference between any of the Ranch Hand categories and the Comparison group when the categorized dioxin-by-current alcohol use interaction was removed from the final model (Table 13-29(f): p>0.17 for all contrasts).

Table 13-29.
Analysis of Cholesterol-HDL Ratio
(Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Mean[a]**	**Difference of Means (95% C.I.)[b]**	**p-Value[c]**
All	*Ranch Hand*	*925*	*5.30*	*0.05 --*	*0.408*
	Comparison	*1,241*	*5.25*		
Officer	Ranch Hand	353	5.07	0.06 --	0.569
	Comparison	491	5.01		
Enlisted Flyer	Ranch Hand	158	5.38	-0.15 --	0.366
	Comparison	193	5.53		
Enlisted Groundcrew	Ranch Hand	414	5.48	0.11 --	0.274
	Comparison	557	5.36		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED						
Occupational Category	**Group**	**n**	**Adj. Mean[a]**	**Difference of Adj. Means (95% C.I.)[b]**	**p-Value[c]**	**Covariate Remarks[d]**
All	*Ranch Hand*	*915*	*5.07*	*0.04 --*	*0.565*	RACE (p<0.001)
	Comparison	*1,224*	*5.03*			OCC (p<0.001)
Officer	Ranch Hand	353	4.82	0.08 --	0.411	ALC (p<0.001)
	Comparison	485	4.74			
Enlisted Flyer	Ranch Hand	155	5.10	-0.20 --	0.199	
	Comparison	193	5.30			
Enlisted Groundcrew	Ranch Hand	407	5.20	0.08 --	0.383	
	Comparison	546	5.12			

[a] Transformed from natural logarithm scale.

[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

[c] P-values based on difference of means on natural logarithm scale.

[d] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 13-29. (Continued)
Analysis of Cholesterol-HDL Ratio
(Continuous)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	172	5.26	5.29	0.035	0.0234 (0.0092)	0.012
Medium	166	5.51	5.51			
High	168	5.58	5.55			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[d]			
Initial Dioxin	n	Adj. Mean[ad]	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
Low	169	5.11**	0.162	0.0142 (0.0105)**	0.178**	INIT*ALC (p=0.006) AGE (p=0.065)
Medium	161	5.17**				RACE*IC (p=0.013) OCC*ALC (p=0.049)
High	163	5.19**				DRKYR*IC (p=0.033) ALC*DC (p=0.024)

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Slope and standard error based on natural logarithm of cholesterol-HDL ratio versus $\log_2$ (initial dioxin).

[d] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interaction ($p \leq 0.05$); adjusted mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-20 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 13-29. (Continued)
Analysis of Cholesterol-HDL Ratio
(Continuous)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,033	5.26	5.25		
Background RH	365	5.07	5.15	-0.10 --	0.253
Low RH	253	5.26	5.24	-0.01 --	0.936
High RH	253	5.64	5.55	0.30 --	0.004
Low plus High RH	506	5.45	5.40	0.14 --	0.073

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Mean[ae]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]	Covariate Remarks
Comparison	1,018	5.08**			DXCAT*ALC (p=0.031) RACE (p=0.001) OCC (p<0.001)
Background RH	363	5.05**	-0.03 --**	0.761**	
Low RH	250	5.07**	-0.00 --**	0.967**	
High RH	249	5.21**	0.14 --**	0.177**	
Low plus High RH	499	5.14**	0.07 --**	0.387**	

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not presented because analysis was performed on natural logarithm scale.

[d] P-value is based on difference of means on natural logarithm scale.

[e] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted mean, difference of adjusted means, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-20 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 13-29. (Continued)
Analysis of Cholesterol-HDL Ratio
(Continuous)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

	Current Dioxin Category Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)		
Model[b]	Low	Medium	High	R^2	Slope (Std. Error)[c]	p-Value
4	5.04 (288)	5.22 (293)	5.62 (290)	0.024	0.0312 (0.0068)	<0.001
5	4.89 (294)	5.29 (294)	5.73 (283)	0.049	0.0384 (0.0058)	<0.001
6[d]	5.15 (293)	5.31 (294)	5.41 (283)	0.226	0.0118 (0.0056)	0.035

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

	Current Dioxin Category Adjusted Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)			
Model[b]	Low	Medium	High	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
4	4.82** (287)	4.99** (290)	5.31** (285)	0.069	0.0281 (0.0069)**	<0.001**	CURR*DC (p=0.030) RACE (p=0.028) ALC (p<0.001)
5	4.68** (292)	5.08** (292)	5.49** (278)	0.091	0.0395 (0.0058)**	<0.001**	CURR*AGE (p=0.044) RACE (p=0.027) ALC (p<0.001)
6[e]	5.16** (291)	5.31** (292)	5.36** (278)	0.283	0.0094 (0.0056)**	0.093**	CURR*DC (p=0.005) ALC (p<0.001)

[a] Transformed from natural logarithm scale.

[b] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[c] Slope and standard error based on natural logarithm of cholesterol-HDL ratio versus log_2 (current dioxin + 1).

[d] Adjusted for log_2 total lipids.

[e] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($p \leq 0.05$); adjusted mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-20 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Without occupation, the adjusted results paralleled the unadjusted results. The adjusted Model 3 analysis detected a significant difference between the high Ranch Hand category and the Comparison group and a marginally significant difference between the low plus high Ranch Hand category and the Comparison group (Appendix Table I-3-19(b): $p=0.006$ and $p=0.078$ respectively).

The unadjusted analyses for Models 4 through 6 revealed a highly significant positive association between HDL cholesterol ratio and current dioxin (Table 13-29(g): $p<0.001$, Est. Slope=0.0312; $p<0.001$, Est. Slope=0.0384; and $p=0.035$, Est. Slope=0.0118 for Models 4, 5, and 6 respectively).

The adjusted analyses for Models 4 and 6 contained a significant interaction between current dioxin and degreasing chemical exposure (Table 13-29(h): $p=0.030$ and $p=0.005$ respectively). Current dioxin-by-age was a significant interaction in the adjusted Model 5 analysis (Table 13-29(h): $p=0.044$). In addition to the current dioxin-by-covariate interactions mentioned above, Models 4 and 5 included race and current alcohol use, whereas Model 6 contained only current alcohol use. Appendix Table I-2-20 presents results stratified by degreasing chemical exposure for Models 4 and 6 and stratified by age for Model 5. After excluding the current dioxin-by-covariate interactions, the results of the adjusted analyses for models 4 and 5 supported the unadjusted findings. There were highly significant positive associations between the HDL-cholesterol ratio and lipid-adjusted current dioxin in Model 4 (Table 13-29(h): $p<0.001$, Adj. Slope=0.0281), and between the HDL-cholesterol ratio and whole-weight current dioxin in Model 5 ($p<0.001$, Adj. Slope=0.0395). Forcing total lipids into the adjusted Model 6 analysis caused the association between the HDL-cholesterol ratio and whole-weight dioxin to become marginally significant ($p=0.093$, Adj. Slope=0.0094). This resulted from the strong correlation between total lipids and the HDL-cholesterol ratio.

Cholesterol-HDL Ratio (Discrete)

The unadjusted and adjusted Model 1 analyses did not reveal a significant group difference in the percentage of individuals with high cholesterol-HDL ratios (Table 13-30(a,b): $p>0.28$ for all contrasts). The adjusted model contained age, occupation, race, and current alcohol use.

The unadjusted Model 2 analysis detected a marginally significant positive association between cholesterol-HDL ratio and initial dioxin (Table 13-30(c): $p=0.081$, Est. RR=1.13, 95% C.I.=[0.98, 1.30]). In contrast with the unadjusted analysis, the adjusted Model 2 analysis did not show a significant association between cholesterol-HDL ratio and initial dioxin (Table 13-30(d): $p=0.547$). The final model contained age, occupation, current alcohol use, and two significant covariate-by-covariate interactions: race-by-industrial chemical exposure and race-by-degreasing chemical exposure.

The unadjusted Model 3 analysis revealed a significant difference between the high Ranch Hand category and the Comparison group in the percentage of participants with elevated cholesterol-HDL ratios (Table 13-30(e): $p=0.009$, Est. RR=1.49, 95% C.I.=[1.11, 2.00]). The unadjusted analysis also detected a marginally significant difference between the

Table 13-30.
Analysis of Cholesterol-HDL Ratio
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent High**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	*Ranch Hand*	*925*	*59.0*	*1.10 (0.93,1.31)*	*0.287*
	Comparison	*1,241*	*56.6*		
Officer	Ranch Hand	353	51.0	1.08 (0.82,1.42)	0.633
	Comparison	491	49.1		
Enlisted Flyer	Ranch Hand	158	63.9	0.96 (0.62,1.50)	0.959
	Comparison	193	64.8		
Enlisted Groundcrew	Ranch Hand	414	64.0	1.16 (0.89,1.51)	0.295
	Comparison	557	60.5		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	*1.07 (0.90,1.28)*	*0.435*	AGE (p=0.096)
Officer	1.10 (0.83,1.44)	0.520	RACE (p=0.001)
Enlisted Flyer	0.90 (0.57,1.40)	0.637	OCC (p<0.001)
Enlisted Groundcrew	1.12 (0.86,1.47)	0.400	ALC (p<0.001)

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 13-30. (Continued)
Analysis of Cholesterol-HDL Ratio
(Discrete)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	172	56.4	1.13 (0.98,1.30)	0.081
Medium	166	68.7		
High	168	64.9		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
499	1.05 (0.89,1.25)	0.547	AGE (p=0.094) OCC (p=0.128) ALC (p<0.001) RACE*IC (p=0.006) RACE*DC (p=0.033)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 13-30. (Continued)
Analysis of Cholesterol-HDL Ratio
(Discrete)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Percent High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,033	57.1		
Background RH	365	52.9	0.93 (0.73,1.18)	0.543
Low RH	253	58.5	1.04 (0.79,1.39)	0.769
High RH	253	68.0	1.49 (1.11,2.00)	0.009
Low plus High RH	506	63.2	1.24 (0.99,1.55)	0.060

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,018			RACE ($p=0.012$) OCC ($p<0.001$) DC ($p=0.137$) ALC ($p<0.001$)
Background RH	363	1.03 (0.80,1.33)	0.803	
Low RH	250	1.02 (0.76,1.37)	0.882	
High RH	249	1.22 (0.89,1.66)	0.216	
Low plus High RH	499	1.11 (0.88,1.39)	0.381	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 13-30. (Continued)
Analysis of Cholesterol-HDL Ratio
(Discrete)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent High/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	52.1 (288)	56.0 (293)	68.6 (290)	1.18 (1.08,1.30)	<0.001
5	47.6 (294)	58.8 (294)	70.7 (283)	1.24 (1.14,1.35)	<0.001
6[c]	47.8 (293)	58.8 (294)	70.7 (283)	1.06 (0.96,1.16)	0.261

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	862	1.15 (1.04,1.27)	0.006	RACE (p=0.115) DC (p=0.007) ALC (p<0.001)
5	862	1.23 (1.12,1.34)	<0.001	IC (p=0.135) DC (p=0.008) ALC (p<0.001)
6[d]	861	1.02 (0.93,1.13)	0.672	DC (p=0.022) ALC (p<0.001)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

low plus high Ranch Hand category and the Comparison group (Table 13-30(e): $p=0.060$, Est. RR=1.24, 95% C.I.=[0.99, 1.55]). The percentages of cholesterol-HDL ratio abnormalities for the high Ranch Hands, low plus high Ranch Hands, and the Comparison group were 68.0 percent, 63.2 percent, and 57.1 percent respectively.

After covariate adjustment, the Model 3 analysis no longer showed any of the Ranch Hand categories to be significantly different from the Comparison group (Table 13-30(f): $p>0.21$ for all contrasts). The final model contained occupation, race, degreasing chemical exposure, and current alcohol use.

Removing occupation from the final model produced a change in the adjusted results. Without occupation, the adjusted Model 3 analysis revealed a significant difference between the high Ranch Hand category and Comparison group (Appendix Table I-3-20(b): $p=0.030$, Adj. RR=1.40, 95% C.I.=[1.03, 1.89]).

The unadjusted analyses for Models 4 and 5 revealed a significant positive association between cholesterol-HDL ratio and current dioxin (Table 13-30(g): $p<0.001$, Est. RR=1.18, 95% C.I.=[1.08, 1.30]; $p<0.001$, Est. RR=1.24, 95% C.I.=[1.14, 1.35]). The unadjusted Model 6 analysis revealed no significant association (Table 13-30(g): $p=0.261$).

The adjusted results for Models 4 through 6 paralleled the unadjusted results. After covariate adjustment, the analysis of Models 4 and 5 revealed a significant association between cholesterol-HDL and current dioxin (Table 13-30(h): $p=0.006$, Adj. RR=1.15, 95% C.I.=[1.04, 1.27]; $p<0.001$, Adj. RR=1.23, 95% C.I.=[1.12, 1.34]). The adjusted Model 6 analysis did not reveal a significant association (Table 13-30(h): $p=0.672$). Each of the adjusted models contained degreasing chemical exposure and current alcohol use. Race was also significant in Model 4, and industrial chemical exposure was significant in Model 5.

Triglycerides (Continuous)

The unadjusted Model 1 analysis did not show a significant overall group difference in the mean levels of triglycerides (Table 13-31(a): $p=0.389$). Stratifying the unadjusted analysis by occupation revealed marginally significant group differences within the officer and enlisted flyer strata (Table 13-31(a): $p=0.058$ and $p=0.074$ respectively). Within the officer stratum, the mean level of triglycerides was higher for the Ranch Hands than the Comparisons (144.96 mg/dl vs. 134.52 mg/dl). However, the Ranch Hands had a lower mean triglyceride level in the enlisted flyer stratum (145.32 mg/dl vs. 162.09 mg/dl).

Group-by-occupation was a significant covariate in the adjusted Model 1 analysis (Table 13-31(b): $p=0.027$). The final model also contained race and the age-by-lifetime alcohol history interaction. The adjusted analysis did not detect a significant overall group difference when the group-by-occupation interaction was removed from the final model (Table 13-31(b): $p=0.362$). For the stratified analysis, the group difference for the officers became significant (Table 13-31(b): $p=0.039$), and the enlisted flyer group contrast remained marginally significant (Table 13-31(b): $p=0.062$).

Table 13-31.
Analysis of Triglycerides (mg/dl)
(Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Mean[a]**	**Difference of Means (95% C.I.)[b]**	**p-Value[c]**
All	*Ranch Hand*	*939*	*147.42*	*3.04 --*	*0.389*
	Comparison	*1,253*	*144.38*		
Officer	Ranch Hand	361	144.96	10.44 --	0.058
	Comparison	495	134.52		
Enlisted Flyer	Ranch Hand	162	145.32	-16.76 --	0.074
	Comparison	196	162.09		
Enlisted Groundcrew	Ranch Hand	416	150.43	2.85 --	0.587
	Comparison	562	147.58		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED						
Occupational Category	**Group**	**n**	**Adj. Mean[a]**	**Difference of Adj. Means (95% C.I.)[b]**	**p-Value[c]**	**Covariate Remarks[d]**
All	*Ranch Hand*	*917*	*131.89***	*2.88 --***	*0.362***	GROUP*OCC (p=0.027)
	Comparison	*1,232*	*129.01***			RACE (p<0.001)
Officer	Ranch Hand	357	125.96**	9.67 --**	0.039**	AGE*DRKYR (p=0.039)
	Comparison	487	116.29**			
Enlisted Flyer	Ranch Hand	156	128.58**	-15.12 --**	0.062**	
	Comparison	195	143.70**			
Enlisted Groundcrew	Ranch Hand	404	135.38**	2.76 --**	0.572**	
	Comparison	550	132.62**			

[a] Transformed from natural logarithm scale.

[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

[c] P-values based on difference of means on natural logarithm scale.

[d] Covariates and associated p-values correspond to final model based on all participants with available data.

** Group-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted mean, difference of adjusted means, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-21 for further analysis of this interaction.

Table 13-31. (Continued)
Analysis of Triglycerides (mg/dl)
(Continuous)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	173	144.60	146.18	0.033	0.0366 (0.0190)	0.055
Medium	170	164.11	164.69			
High	172	163.20	160.85			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[d]			
Initial Dioxin	n	Adj. Mean[ad]	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
Low	173	128.27**	0.065	0.0403 (0.0218)**	0.065**	INIT*OCC (p=0.031) RACE (p=0.003)
Medium	170	144.14**				
High	172	141.84**				

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Slope and standard error based on natural logarithm of triglycerides versus $\log_2$ (initial dioxin).

[d] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-21 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 13-31. (Continued)
Analysis of Triglycerides (mg/dl)
(Continuous)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,043	145.90	145.69		
Background RH	369	134.41	139.43	-6.26 --	0.188
Low RH	257	147.66	145.96	0.27 --	0.962
High RH	258	166.86	161.08	15.39 --	0.008
Low plus High RH	515	156.99	153.33	7.64 --	0.083

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Mean[ae]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]	Covariate Remarks
Comparison	1,025	130.78			RACE (p<0.001) OCC (p=0.013) AGE*DRKYR (p=0.013)
Background RH	362	127.25	-3.53 --	0.423	
Low RH	251	132.05	1.27 --	0.802	
High RH	251	142.50	11.72 --	0.031	
Low plus High RH	502	137.17	6.39 --	0.112	

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not presented because analysis was performed on natural logarithm scale.

[d] P-value is based on difference of means on natural logarithm scale.

[e] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 13-31. (Continued)
Analysis of Triglycerides (mg/dl)
(Continuous)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED						
	Current Dioxin Category Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)		
Model[b]	Low	Medium	High	R^2	Slope (Std. Error)[c]	p-Value
4	132.26 (290)	144.11 (298)	166.78 (296)	0.027	0.0649 (0.0130)	<0.001
5	123.83 (294)	145.27 (297)	177.21 (293)	0.066	0.0888 (0.0109)	<0.001
6[d]	141.65 (293)	147.20 (297)	152.67 (293)	0.380	0.0196 (0.0096)	0.041

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED							
	Current Dioxin Category Adjusted Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)			
Model[b]	Low	Medium	High	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
4	114.92** (290)	127.79** (298)	151.18** (296)	0.048	0.0729 (0.0149)**	<0.001**	CURR*OCC (p=0.035) RACE (p=0.002)
5	106.25** (290)	128.43** (290)	164.67** (284)	0.116	0.1049 (0.0124)**	<0.001**	CURR*OCC (p<0.001) CURR*DRKYR (p=0.027) RACE (p=0.002) AGE*DRKYR (p=0.031)
6[e]	128.58** (289)	136.68** (290)	145.26** (284)	0.401	0.0298 (0.0110)**	0.007**	CURR*OCC (p=0.041) CURR*DRKYR (p=0.035) RACE (p=0.024) ALC (p=0.099)

[a] Transformed from natural logarithm scale.

[b] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[c] Slope and standard error based on natural logarithm of triglycerides versus log_2 (current dioxin + 1).

[d] Adjusted for log_2 total lipids.

[e] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interactions ($p \leq 0.05$); adjusted mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table I-2-21 for further analysis of these interactions.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

The unadjusted Model 2 results showed a marginally significant positive association between triglycerides and initial dioxin (Table 13-31(c): p=0.055, Est. Slope=0.0366). The adjusted analysis of Model 2 contained a significant interaction between initial dioxin and occupation (Table 13-31(d): p=0.031). Appendix Table I-2-21 displays adjusted results stratified by occupation. The final model also included race. The association between triglycerides and initial dioxin remained marginally significant after the initial dioxin-by-occupation interaction was removed from the adjusted analysis (Table 13-31(d): p=0.065, Adj. Slope=0.0403).

The unadjusted Model 3 analysis showed a significant difference between the high Ranch Hands and Comparisons and a marginally significant difference between the low plus high Ranch Hands and Comparisons (Table 13-31(e): p=0.008 and p=0.083 respectively). The mean levels of triglycerides, adjusted for percent body fat at the time of duty in SEA and the change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, for the high Ranch Hands, low plus high Ranch Hand category, and the Comparison group were 161.08 mg/dl, 153.33 mg/dl, and 145.69 mg/dl respectively.

After adjusting for race, occupation, and the age-by-lifetime alcohol history interaction, the adjusted analysis detected a significant difference between the high Ranch Hand category and the Comparison group (Table 13-31(f): p=0.031). The contrast between the low plus high Ranch Hand category and the Comparison group became nonsignificant (p=0.112). After deletion of occupation from the final model, the contrast between the low plus high Ranch Hand category and the Comparison group became significant (Appendix Table I-3-21(b): p=0.040).

Each of the unadjusted analyses for Models 4 through 6 revealed a significant association between triglycerides and current dioxin (Table 13-31(g): p<0.001, Est. Slope=0.0649; p<0.001, Est. Slope=0.0888; and p=0.041, Est. Slope=0.0196 for Models 4, 5, and 6 respectively).

The interaction between current dioxin and occupation was significant in each of the adjusted analyses of Models 4, 5, and 6 (Table 13-31(h): p=0.035, p<0.001, and p=0.041 respectively). The current dioxin-by-lifetime alcohol history interaction also was significant in Models 5 and 6 (Table 13-31(h): p=0.027 and p=0.035 for Models 4 and 5). Appendix Table I-2-21 presents adjusted results stratified by occupation and lifetime alcohol history. In addition to the current dioxin-by-covariate interactions, Model 4 included race; Model 5 contained race and the age-by-lifetime alcohol history interaction; and Model 6 included race and current alcohol use. Without the current dioxin-by-covariate interactions, the adjusted analyses detected a significant positive association between triglycerides and current dioxin (Table 13-13(h): p<0.001, Adj. Slope=0.0729; p<0.001, Adj. Slope=0.1049; and p=0.007, Adj. Slope=0.0298 for Models 4, 5, and 6 respectively).

Triglycerides (Discrete)

The unadjusted Model 1 analysis did not reveal a significant overall group difference in the percentage of individuals having high triglyceride levels (Table 13-32(a): p=0.179). Stratifying the analysis by occupation revealed a marginally significant group difference

within the officer stratum (Table 13-32(a): p=0.063, Est. RR=1.58, 95% C.I.=[1.00, 2.50]). For the officers, the percentage of triglyceride abnormalities was higher for the Ranch Hands than for the Comparisons (11.9% vs. 7.9%).

After adjusting for age, race, and industrial chemical exposure, the Model 1 analysis did not reveal a significant overall group difference (Table 13-32(b): p=0.162). However, the group contrast within the officer stratum became significant (Table 13-32(b): p=0.050, Adj. RR=1.58, 95% C.I.=[1.00, 2.49]).

The unadjusted and adjusted Model 2 analyses did not show a significant association between triglycerides and initial dioxin (Table 13-32(c,d): p>0.15 for both analyses). Race and degreasing chemical exposure were significant in the adjusted analysis.

The unadjusted Model 3 analysis revealed a marginally significant difference between the high Ranch Hand category and the Comparison group (Table 13-32(e): p=0.071, Est. RR=1.46, 95% C.I.=[0.97, 2.19]). Ranch Hands had a higher percentage of individuals with high triglyceride levels than Comparisons (14.7% vs. 9.7%).

Adjusting for age and race caused the contrast between the high Ranch Hands and the Comparison group to become significant (Table 13-32(f): p=0.036, Adj. RR=1.56, 95% C.I.=[1.03, 2.36]). The adjusted Model 3 analysis did not reveal any other significant contrasts involving the Comparisons.

The unadjusted results for Models 4 and 5 revealed a significant positive association between triglycerides and current dioxin (Table 13-32(g): p=0.013, Est. RR=1.19, 95% C.I.=[1.04, 1.37] and p<0.001, Est. RR=1.35, 95% C.I.=[1.19, 1.53] for Models 4 and 5 respectively). The unadjusted Model 6 analysis did not reveal a significant association (Table 13-32(g): p=0.949).

The adjusted analyses of Models 4 and 5 revealed a significant positive association between triglycerides and current dioxin (Table 13-32(h): p=0.002, Adj. RR=1.32, 95% C.I.=[1.11, 1.57] and p<0.001, Adj. RR=1.60, 95% C.I.=[1.35, 1.90]), but the adjusted Model 6 analysis did not show a significant association (Table 13-32(h): p=0.293). The analyses of Models 4 and 5 contained occupation and race, whereas the adjusted Model 6 analysis contained the occupation-by-degreasing chemical exposure interaction.

Creatine Kinase (Continuous)

The unadjusted Model 1 analysis did not show a significant group difference in the mean levels of creatine kinase (Table 13-33(a): p>0.14 for all contrasts). The adjusted Model 1 analysis contained a significant interaction between group and race. Appendix Table I-2-22 presents the adjusted results stratified by race. The adjusted analysis also includes five covariate-by-covariate interactions: age-by-lifetime alcohol history, current alcohol use-by-degreasing chemical exposure, current alcohol use-by-lifetime alcohol history, current alcohol use-by-industrial chemical exposure, and race-by-lifetime alcohol history. The adjusted analysis did not reveal a significant group difference after removing the group-by-race interaction from the final model (Table 13-33(b): p>0.29 for all contrasts).

Table 13-32.
Analysis of Triglycerides
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent High**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	*Ranch Hand*	*939*	*11.2*	*1.22 (0.93,1.61)*	*0.179*
	Comparison	*1,253*	*9.3*		
Officer	Ranch Hand	361	11.9	1.58 (1.00,2.50)	0.063
	Comparison	495	7.9		
Enlisted Flyer	Ranch Hand	162	13.6	1.24 (0.66,2.34)	0.607
	Comparison	196	11.2		
Enlisted Groundcrew	Ranch Hand	416	9.6	0.96 (0.63,1.47)	0.942
	Comparison	562	10.0		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	*1.22 (0.92,1.61)*	*0.162*	AGE (p=0.046) RACE (p=0.013) IC (p=0.125)
Officer	1.58 (1.00,2.49)	0.050	
Enlisted Flyer	1.21 (0.64,2.29)	0.549	
Enlisted Groundcrew	0.97 (0.63,1.48)	0.877	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 13-32. (Continued)
Analysis of Triglycerides
(Discrete)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	173	9.2	1.13 (0.93,1.37)	0.211
Medium	170	16.5		
High	172	12.8		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
515	1.15 (0.95,1.40)	0.156	RACE (p=0.067) DC (p=0.079)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 13-32. (Continued)
Analysis of Triglycerides
(Discrete)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	**n**	**Percent High**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,043	9.7		
Background RH	369	8.9	1.04 (0.68,1.58)	0.862
Low RH	257	10.9	1.10 (0.70,1.72)	0.685
High RH	258	14.7	1.46 (0.97,2.19)	0.071
Low plus High RH	515	12.8	1.28 (0.91,1.78)	0.152

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	**n**	**Adj. Relative Risk (95% C.I.)[ac]**	**p-Value**	**Covariate Remarks**
Comparison	1,043			AGE (p=0.018) RACE (p=0.016)
Background RH	369	0.99 (0.65,1.50)	0.959	
Low RH	257	1.07 (0.68,1.69)	0.759	
High RH	258	1.56 (1.03,2.36)	0.036	
Low plus High RH	515	1.31 (0.93,1.83)	0.121	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 13-32. (Continued)
Analysis of Triglycerides
(Discrete)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent High/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	8.3 (290)	10.4 (298)	14.9 (296)	1.19 (1.04,1.37)	0.013
5	5.8 (294)	10.1 (297)	17.7 (293)	1.35 (1.19,1.53)	<0.001
6[c]	5.8 (293)	10.1 (297)	17.7 (293)	1.01 (0.86,1.17)	0.949

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	884	1.32 (1.11,1.57)	0.002	RACE (p=0.030) OCC (p=0.088)
5	884	1.60 (1.35,1.90)	<0.001	RACE (p=0.056) OCC (p=0.001)
6[d]	883	1.11 (0.92,1.33)	0.293	OCC*DC (p=0.049)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for $\log_2$ total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for $\log_2$ total lipids.

[d] Adjusted for $\log_2$ total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 13-33.
Analysis of Creatine Kinase (U/L)
(Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Mean[a]**	**Difference of Means (95% C.I.)[b]**	**p-Value[c]**
All	*Ranch Hand*	*939*	*128.05*	*-1.25 --*	*0.679*
	Comparison	*1,253*	*129.31*		
Officer	Ranch Hand	361	127.61	2.88 --	0.535
	Comparison	495	124.74		
Enlisted Flyer	Ranch Hand	162	117.32	-10.20 --	0.146
	Comparison	196	127.51		
Enlisted Groundcrew	Ranch Hand	416	132.89	-1.23 --	0.799
	Comparison	562	134.12		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED						
Occupational Category	**Group**	**n**	**Adj. Mean[a]**	**Difference of Adj. Means (95% C.I.)[b]**	**p-Value[c]**	**Covariate Remarks[d]**
All	*Ranch Hand*	*917*	*168.64***	*-1.08 --***	*0.780***	GROUP*RACE (p<0.001)
	Comparison	*1,232*	*169.72***			AGE*DRKYR (p=0.017)
Officer	Ranch Hand	357	175.29**	4.62 --**	0.464**	ALC*DC (p=0.022)
	Comparison	487	170.67**			ALC*DRKYR (p=0.038)
Enlisted Flyer	Ranch Hand	156	158.25**	-9.52 --**	0.299**	ALC*IC (p=0.021)
	Comparison	195	167.76**			RACE*DRKYR (p=0.037)
Enlisted Groundcrew	Ranch Hand	404	167.41**	-2.53 --**	0.663**	
	Comparison	550	169.93**			

[a] Transformed from natural logarithm scale.

[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

[c] P-values based on difference of means on natural logarithm scale.

[d] Covariates and associated p-values correspond to final model based on all participants with available data.

** Group-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted mean, difference of adjusted means, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-22 for further analysis of this interaction.

Table 13-33. (Continued)
Analysis of Creatine Kinase (U/L)
(Continuous)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	173	128.97	130.38	0.032	0.0114 (0.0173)	0.512
Medium	170	125.22	125.65			
High	172	139.43	137.45			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[d]			
Initial Dioxin	n	Adj. Mean[ad]	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
Low	170	156.53	0.124	0.0217 (0.0167)	0.196	RACE*DRKYR ($p<0.001$)
Medium	165	153.93				
High	167	169.59				

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Slope and standard error based on natural logarithm of creatine kinase versus $\log_2$ (initial dioxin).

[d] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 13-33. (Continued)
Analysis of Creatine Kinase (U/L)
(Continuous)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED					
Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,043	128.46	128.30		
Background RH	369	123.12	126.97	-1.33 --	0.750
Low RH	257	129.04	127.95	-0.35 --	0.941
High RH	258	133.17	129.17	0.87 --	0.857
Low plus High RH	515	131.09	128.56	0.26 --	0.945

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED					
Dioxin Category	n	Adj. Mean[ae]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]	Covariate Remarks
Comparison	1,025	170.02**			DXCAT*RACE (p=0.013) DXCAT*DRKYR (p=0.020) AGE (p=0.002) OCC*DRKYR (p=0.039) RACE*DRKYR (p=0.049)
Background RH	362	168.64**	-1.38 --**	0.801**	
Low RH	251	167.25**	-2.77 --**	0.650**	
High RH	251	172.64**	2.61 --**	0.684**	
Low plus High RH	502	169.92**	-0.10 --**	0.983**	

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not presented because analysis was performed on natural logarithm scale.

[d] P-value is based on difference of means on natural logarithm scale.

[e] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interactions ($0.01 < p \leq 0.05$); adjusted mean, difference of adjusted means, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table I-2-22 for further analysis of these interactions.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 13-33. (Continued)
Analysis of Creatine Kinase (U/L)
(Continuous)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED						
	Current Dioxin Category Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)		
Model[b]	Low	Medium	High	R^2	Slope (Std. Error)[c]	p-Value
4	121.20 (290)	129.41 (298)	132.63 (296)	0.006	0.0278 (0.0116)	0.017
5	120.67 (294)	131.43 (297)	131.27 (293)	0.007	0.0253 (0.0100)	0.011
6[d]	121.11 (293)	131.44 (297)	131.23 (293)	0.006	0.0237 (0.0107)	0.027

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED							
	Current Dioxin Category Adjusted Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)			
Model[b]	Low	Medium	High	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
4	135.67 (287)	146.74 (290)	154.76 (287)	0.089	0.0392 (0.0130)	0.003	AGE (p=0.139) DC (p=0.135) RACE*OCC (p=0.033) RACE*DRKYR (p<0.001)
5	136.29 (290)	148.17 (290)	153.20 (284)	0.090	0.0350 (0.0110)	0.002	AGE (p=0.122) DC (p=0.124) RACE*OCC (p=0.035) RACE*DRKYR (p<0.001)
6[e]	137.18 (289)	148.32 (290)	152.79 (284)	0.088	0.0324 (0.0119)	0.006	AGE (p=0.127) DC (p=0.131) RACE*OCC (p=0.034) RACE*DRKYR (p<0.001)

[a] Transformed from natural logarithm scale.

[b] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[c] Slope and standard error based on natural logarithm of creatine kinase versus log_2 (current dioxin + 1).

[d] Adjusted for log_2 total lipids.

[e] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

The unadjusted and adjusted Model 2 analyses did not show a significant association between creatine kinase and initial dioxin (Table 13-33(c,d): $p>0.19$ for both analyses). The adjusted analysis contained the race-by-lifetime alcohol history interaction.

Displayed in Table 13-33(e), the unadjusted Model 3 analysis of creatine kinase did not show a significant difference between any of the Ranch Hand categories and the Comparison group (Table 13-33(e): $p>0.75$). Categorized dioxin-by-race and categorized dioxin-by-lifetime alcohol history were significant interactions in the adjusted Model 3 analysis (Table 13-33(f): $p=0.013$ and $p=0.020$ respectively). Appendix Table I-2-22 presents adjusted results stratified separately by race and lifetime alcohol history. The final model also contained age and two covariate-by-covariate interactions: occupation-by-lifetime alcohol history and race-by-lifetime alcohol history. The adjusted analysis did not show any of the Ranch Hand categories to be significantly different from the Comparison group when the two categorized dioxin-by-covariate interactions were removed from the final model (Table 13-33(f): $p>0.65$ for all contrasts).

Each of the unadjusted analyses for Models 4 through 6 detected a significant positive association between creatine kinase and current dioxin (Table 13-33(g): $p=0.017$, Est. Slope=0.0278; $p=0.011$, Est. Slope=0.0253; and $p=0.027$, Est. Slope=0.0237 for Models 4, 5, and 6 respectively). Similar to the unadjusted analyses, the adjusted analyses for Models 4 through 6 revealed a significant positive association between creatine kinase and current dioxin (Table 13-33(h): $p=0.003$, Adj. Slope=0.0392; $p=0.002$, Adj. Slope=0.0350; and $p=0.006$, Adj. Slope=0.0324 for Models 4, 5, and 6 respectively). Each of the adjusted analyses contained age, degreasing chemical exposure and two covariate-by-covariate interactions, race-by-occupation and race-by-lifetime alcohol history.

Creatine Kinase (Discrete)

The unadjusted Model 1 analysis did not reveal a significant group difference in the percentage of participants with high creatine kinase levels (Table 13-34(a): $p>0.38$ for all contrasts). The adjusted analysis contained a significant group-by-race interaction (Table 13-34(b): $p=0.005$). Appendix Table I-2-23 presents the adjusted results stratified by race. The race-by-current alcohol use and current alcohol use-by-degreasing chemical exposure interactions were significant in the final model. The adjusted analysis did not reveal a significant group difference when the group-by-race interaction was removed from the Model 1 analysis (Table 13-34(b): $p>0.30$ for all analyses).

The unadjusted and adjusted Model 2 analyses did not show a significant association between creatine kinase and initial dioxin (Table 13-34(c): $p>0.51$ for both analyses). The adjusted analysis contained three covariate-by-covariate interactions: occupation-by-current alcohol use, age-by-lifetime alcohol history, and race-by-lifetime alcohol history.

The unadjusted Model 3 results did not show any of the Ranch Hand categories to be significantly different from the Comparison group (Table 13-34(e): $p>0.81$ for all contrasts). Categorized dioxin-by-race and categorized dioxin-by-lifetime alcohol history were significant interactions in the adjusted Model 3 analysis (Table 13-34(f): $p=0.006$ and $p=0.004$ respectively). Appendix Table I-2-23 displays adjusted results stratified separately by race

Table 13-34.
Analysis of Creatine Kinase
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Percent High	Est. Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*939*	*14.1*	*1.02 (0.80,1.30)*	*0.916*
	Comparison	*1,253*	*13.8*		
Officer	Ranch Hand	361	13.9	1.21 (0.81,1.82)	0.410
	Comparison	495	11.7		
Enlisted Flyer	Ranch Hand	162	11.1	0.72 (0.38,1.35)	0.384
	Comparison	196	14.8		
Enlisted Groundcrew	Ranch Hand	416	15.4	1.01 (0.71,1.43)	0.999
	Comparison	562	15.3		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	*1.02 (0.79,1.32)***	*0.871***	GROUP*RACE (p=0.005) RACE*ALC (p<0.001) ALC*DC (p=0.002)
Officer	1.24 (0.82,1.89)**	0.308**	
Enlisted Flyer	0.74 (0.38,1.45)**	0.384**	
Enlisted Groundcrew	0.97 (0.67,1.41)**	0.878**	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

** Group-by-covariate interaction ($p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-23 for further analysis of this interaction.

Table 13-34. (Continued)
Analysis of Creatine Kinase
(Discrete)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	173	13.3	1.01 (0.84,1.21)	0.914
Medium	170	12.4		
High	172	18.0		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
502	1.08 (0.85,1.37)	0.519	OCC*ALC (p=0.019) AGE*DRKYR (p<0.001) RACE*DRKYR (p<0.001)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 13-34. (Continued)
Analysis of Creatine Kinase
(Discrete)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	**n**	**Percent High**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,043	13.6		
Background RH	369	12.5	1.04 (0.72,1.49)	0.845
Low RH	257	13.6	0.95 (0.64,1.43)	0.818
High RH	258	15.5	1.04 (0.70,1.53)	0.851
Low plus High RH	515	14.6	1.00 (0.73,1.36)	0.982

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	**n**	**Adj. Relative Risk (95% C.I.)[ac]**	**p-Value**	**Covariate Remarks**
Comparison	1,025			DXCAT*RACE (p=0.006) DXCAT*DRKYR (p=0.004) OCC*DRKYR (p=0.003) RACE*ALC (p=0.002) IC*ALC (p=0.037) DC*ALC (p=0.002)
Background RH	362	1.04 (0.70,1.54)**	0.835**	
Low RH	251	0.84 (0.54,1.30)**	0.425**	
High RH	251	1.19 (0.78,1.83)**	0.417**	
Low plus High RH	502	1.00 (0.72,1.39)**	0.997**	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interactions ($p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table I-2-23 for further analysis of these interactions.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 13-34. (Continued)
Analysis of Creatine Kinase
(Discrete)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent High/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	12.4 (290)	13.4 (298)	15.2 (296)	1.08 (0.95,1.23)	0.254
5	11.9 (294)	14.5 (297)	14.7 (293)	1.06 (0.95,1.19)	0.305
6[c]	11.9 (293)	14.5 (297)	14.7 (293)	1.07 (0.95,1.21)	0.248

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	864	1.16 (0.99,1.37)	0.070	OCC*ALC (p=0.022) RACE*DRKYR (p=0.003) AGE*DRKYR (p=0.001)
5	864	1.13 (0.98,1.30)	0.097	OCC*ALC (p=0.023) RACE*DRKYR (p=0.004) AGE*DRKYR (p=0.001)
6[d]	863	1.14 (0.98,1.33)	0.090	OCC*ALC (p=0.022) RACE*DRKYR (p=0.003) AGE*DRKYR (p=0.002)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for $\log_2$ total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for $\log_2$ total lipids.

[d] Adjusted for $\log_2$ total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

and lifetime alcohol history. The adjusted analysis also contained four covariate-by-covariate interactions: occupation-by-lifetime alcohol history, race-by-current alcohol use, industrial chemical exposure-by-current alcohol use, and degreasing chemical exposure-by-current alcohol use. The adjusted Model 3 analysis did not show a significant difference between any of the Ranch Hand categories and the Comparison group after the categorized dioxin-by-covariate interactions were removed from the final model (Table 13-34(f): $p>0.41$ for all contrasts).

The unadjusted analyses for Models 4 through 6 did not reveal a significant association between creatine kinase and current dioxin (Table 13-34: $p>0.24$ for all analyses). In contrast to the unadjusted analyses, the adjusted analyses for Models 4 through 6 detected marginally significant positive associations between creatine kinase and current dioxin (Table 13-34(h); $p=0.070$, Adj. RR=1.16, 95% C.I.=[0.99, 1.37]; $p=0.097$, Adj. RR=1.13, 95% C.I.=[0.98, 1.30]; and $p=0.090$, Adj. RR=1.14, 95% C.I.=[0.98, 1.33] for Models 4, 5, and 6 respectively). Each of the final models contained three covariate-by-covariate interactions: occupation-by-current alcohol use, race-by-lifetime alcohol history, and age-by-lifetime alcohol history.

Removing occupation from the analyses of Models 4 through 6 changed the adjusted results. Without occupation, the adjusted analyses did not show a significant association between creatine kinase and current dioxin (Appendix Table I-3-24(c): $p>0.28$ for all analyses).

Serum Amylase (Continuous)

The unadjusted Model 1 analysis did not show a significant group difference in the mean levels of serum amylase (Table 13-35(a): $p>0.10$ for all contrasts). After adjusting for age and three covariate-by-covariate interactions (race-by-degreasing chemical exposure, current alcohol use-by-occupation, and current alcohol use-by-industrial chemical exposure), the adjusted analysis did not detect a significant overall group difference (Table 13-35(b): $p=0.895$). However, stratifying the adjusted analysis by occupation revealed a marginally significant group difference within the officer stratum (Table 13-35(b): $p=0.058$). For the officers, the adjusted mean level of serum amylase was lower for Ranch Hands than Comparisons (81.74 U/L vs. 85.58 U/L).

The results from the unadjusted Model 2 analysis revealed a significant inverse association between serum amylase and initial dioxin (Table 13-35(c): $p=0.014$, Est. Slope=-0.0290). After covariate adjustment, the Model 2 analysis also detected a significant inverse association between serum amylase and initial dioxin (Table 13-35(d): $p=0.027$, Adj. Slope=-0.0273). The final model contained current alcohol use and two covariate-by-covariate interactions: age-by-degreasing chemical exposure and race-by-lifetime alcohol history.

The unadjusted Model 3 analysis revealed a marginally significant difference between the low Ranch Hands and the Comparison group (Table 13-35(e): $p=0.092$). The mean levels of serum amylase, adjusted for percent body fat at the time of duty in SEA and the change in percent of body fat from the time of duty in SEA to the date of the blood draw for

Table 13-35.
Analysis of Serum Amylase (U/L)
(Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	*Ranch Hand*	*939*	*73.27*	*-0.30 --*	*0.791*
	Comparison	*1,253*	*73.57*		
Officer	Ranch Hand	361	72.08	-2.93 --	0.109
	Comparison	495	75.01		
Enlisted Flyer	Ranch Hand	162	73.89	2.22 --	0.394
	Comparison	196	71.67		
Enlisted Groundcrew	Ranch Hand	416	74.07	1.08 --	0.528
	Comparison	562	72.99		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED						
Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]	Covariate Remarks[d]
All	*Ranch Hand*	*929*	*82.89*	*-0.17 --*	*0.895*	AGE ($p<0.001$)
	Comparison	*1,235*	*83.05*			RACE*DC ($p=0.033$)
Officer	Ranch Hand	361	81.74	-3.84 --	0.058	ALC*OCC ($p=0.031$)
	Comparison	488	85.58			ALC*IC ($p=0.043$)
Enlisted Flyer	Ranch Hand	159	82.86	2.05 --	0.503	
	Comparison	196	80.81			
Enlisted Groundcrew	Ranch Hand	409	84.79	2.25 --	0.238	
	Comparison	551	82.54			

[a] Transformed from natural logarithm scale.

[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

[c] P-values based on difference of means on natural logarithm scale.

[d] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 13-35. (Continued)
Analysis of Serum Amylase (U/L)
(Continuous)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	173	77.45	76.76	0.058	-0.0290 (0.0118)	0.014
Medium	170	71.43	71.20			
High	172	70.12	70.99			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[d]			
Initial Dioxin	n	Adj. Mean[ad]	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
Low	170	84.74	0.132	-0.0273 (0.0123)	0.027	ALC (p=0.024) AGE*DC (p=0.036) RACE*DRKYR (p=0.011)
Medium	165	78.98				
High	167	79.36				

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Slope and standard error based on natural logarithm of serum amylase versus $\log_2$ (initial dioxin).

[d] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 13-35. (Continued)
Analysis of Serum Amylase (U/L)
(Continuous)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,043	73.57	73.63		
Background RH	369	73.36	71.73	-1.90 --	0.223
Low RH	257	76.11	76.74	3.11 --	0.092
High RH	258	69.93	71.39	-2.24 --	0.208
Low plus High RH	515	72.95	74.02	0.39 --	0.783

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Mean[ae]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]	Covariate Remarks
Comparison	1,027	81.69			RACE ($p<0.001$) ALC ($p=0.004$) AGE*DC ($p=0.047$) OCC*IC ($p=0.037$)
Background RH	367	79.25	-2.44 --	0.162	
Low RH	254	84.37	2.69 --	0.184	
High RH	254	80.36	-1.33 --	0.514	
Low plus High RH	508	82.34	0.65 --	0.676	

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not presented because analysis was performed on natural logarithm scale.

[d] P-value is based on difference of means on natural logarithm scale.

[e] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 13-35. (Continued)
Analysis of Serum Amylase (U/L)
(Continuous)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED						
	Current Dioxin Category Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)		
Model[b]	Low	Medium	High	R^2	Slope (Std. Error)[c]	p-Value
4	74.05 (290)	74.46 (298)	70.91 (296)	0.005	-0.0171 (0.0082)	0.037
5	73.77 (294)	75.23 (297)	70.41 (293)	0.006	-0.0164 (0.0070)	0.019
6[d]	72.85 (293)	75.14 (297)	71.31 (293)	0.011	-0.0104 (0.0075)	0.170

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED							
	Current Dioxin Category Adjusted Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)			
Model[b]	Low	Medium	High	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
4	84.74 (290)	83.30 (298)	78.75 (296)	0.045	-0.0238 (0.0092)	0.010	AGE (p=0.013) RACE (p<0.001) OCC (p=0.060)
5	84.22 (294)	83.84 (297)	78.16 (293)	0.046	-0.0220 (0.0078)	0.005	AGE (p=0.012) RACE (p<0.001) OCC (p=0.051)
6[e]	82.91 (293)	83.46 (297)	78.95 (293)	0.049	-0.0160 (0.0084)	0.058	AGE (p=0.008) RACE (p<0.001) OCC (p=0.072)

[a] Transformed from natural logarithm scale.

[b] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[c] Slope and standard error based on natural logarithm of serum amylase versus log_2 (current dioxin + 1).

[d] Adjusted for log_2 total lipids.

[e] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

dioxin, for the low Ranch Hand category and the Comparison group were 76.74 mg/dl and 73.63 mg/dl respectively. By contrast, the adjusted Model 3 analysis did not show any of the Ranch Hand categories to be significantly different from the Comparison group (Table 13-35(f): p>0.16 for all contrasts). The final model contained race, current alcohol use, and two covariate-by-covariate interactions: age-by-degreasing chemical exposure and occupation-by-industrial chemical exposure.

For Models 4 and 5, the unadjusted analyses revealed a significant inverse association between serum amylase and current dioxin (Table 13-35(g): p=0.037, Est. Slope=-0.0171 and p=0.019, Est. Slope=-0.0164 respectively). The unadjusted Model 6 analysis did not show a significant association (Table 13-35(g): p=0.170).

The adjusted results paralleled the unadjusted results for Models 4 and 5. After covariate adjustment, the Model 4 and 5 analyses revealed a significant inverse association between serum amylase and current dioxin (Table 13-35(h): p=0.010, Adj. Slope=-0.0238 and p=0.005, Adj. Slope=-0.0220 respectively). In contrast to the unadjusted results, the adjusted Model 6 analysis detected a marginally significant inverse association between serum amylase and current dioxin (Table 13-35(h): p=0.058, Adj. Slope=-0.0160). Each of the adjusted analyses contained age, race, and occupation.

Deleting occupation from the analyses of Models 4 through 6 produced a change in the adjusted results. For Models 4 and 5, the adjusted analysis detected only a marginally significant inverse association between serum amylase and current dioxin (Appendix Table I-3-25(b): p=0.096, Adj. Slope=-0.0137 and p=0.053, Adj. Slope=-0.0136 respectively). The adjusted Model 6 analysis without occupation did not show a significant association between serum amylase and current dioxin (Appendix Table I-3-25(b): p=0.321).

Serum Amylase (Discrete)

The unadjusted and adjusted Model 1 analyses did not reveal a significant group difference in the percentage of participants having high serum amylase levels (Table 13-36(a,b): p>0.20 for all contrasts). The adjusted model contained age, race, and occupation.

The results from the unadjusted Model 2 analysis did not detect a significant association between serum amylase and initial dioxin (Table 13-36(c): p=0.189). Initial dioxin-by-age was a significant interaction in the adjusted Model 2 analysis (Table 13-36(c): p=0.007). Appendix Table I-2-24 displays adjusted results stratified by age. The final model also contained race, degreasing chemical exposure, current alcohol use, and an interaction between occupation and age. After the initial dioxin-by-age interaction was removed from the final model, the adjusted analysis did not find a significant association between serum amylase and initial dioxin (p=0.558).

The unadjusted Model 3 analysis did not show any of the Ranch Hand categories to be significantly different from the Comparison group (Table 13-36(d): p>0.13 for all contrasts). The interaction between categorized dioxin and race was significant in the adjusted analysis of Model 3 (Table 13-36(f): p=0.029). Appendix Table I-2-24 displays

Table 13-36.
Analysis of Serum Amylase
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	Group	n	Percent High	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***939***	***6.4***	***0.90 (0.64,1.27)***	***0.618***
	Comparison	***1,253***	***7.0***		
Officer	Ranch Hand	361	6.9	0.74 (0.45,1.24)	0.310
	Comparison	495	9.1		
Enlisted Flyer	Ranch Hand	162	3.1	1.01 (0.30,3.37)	0.999
	Comparison	196	3.1		
Enlisted Groundcrew	Ranch Hand	416	7.2	1.10 (0.67,1.82)	0.798
	Comparison	562	6.6		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	***0.90 (0.64,1.27)***	***0.555***	AGE (p=0.003) RACE (p<0.001) OCC (p<0.001)
Officer	0.72 (0.43,1.20)	0.203	
Enlisted Flyer	1.05 (0.31,3.57)	0.934	
Enlisted Groundcrew	1.11 (0.67,1.85)	0.687	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 13-36. (Continued)
Analysis of Serum Amylase
(Discrete)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	173	8.1	0.82 (0.60,1.12)	0.189
Medium	170	4.1		
High	172	5.2		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
508	0.89 (0.61,1.31)**	0.558**	INIT*AGE (p=0.007) RACE (p<0.001) DC (p=0.030) ALC (p=0.070) OCC*AGE (p=0.003)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interaction ($p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-24 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 13-36. (Continued)
Analysis of Serum Amylase
(Discrete)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,043	7.9		
Background RH	369	6.8	0.77 (0.48,1.23)	0.273
Low RH	257	7.0	0.91 (0.53,1.54)	0.719
High RH	258	4.7	0.62 (0.33,1.16)	0.137
Low plus High RH	515	5.8	0.77 (0.50,1.19)	0.232

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,043			DXCAT*RACE (p=0.029) AGE (p=0.003) OCC (p<0.001) DC (p=0.107)
Background RH	369	0.71 (0.44,1.15)**	0.160**	
Low RH	257	0.82 (0.47,1.42)**	0.481**	
High RH	258	0.74 (0.38,1.44)**	0.379**	
Low plus High RH	515	0.79 (0.50,1.24)**	0.304**	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-24 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 13-36. (Continued)
Analysis of Serum Amylase
(Discrete)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent High/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	5.9 (290)	7.7 (298)	5.1 (296)	0.91 (0.75,1.11)	0.343
5	6.5 (294)	8.1 (297)	4.1 (293)	0.92 (0.78,1.08)	0.309
6[c]	6.5 (293)	8.1 (297)	4.1 (293)	0.96 (0.81,1.14)	0.628

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	884	0.90 (0.72,1.14)	0.394	AGE (p=0.001) RACE (p<0.001) OCC (p=0.041) DC (p=0.015)
5	884	0.91 (0.76,1.10)	0.340	AGE (p=0.001) RACE (p<0.001) OCC (p=0.041) DC (p=0.014)
6[d]	883	0.95 (0.78,1.17)	0.660	AGE (p=0.001) RACE (p<0.001) OCC (p=0.037) DC (p=0.012)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

adjusted results stratified by race. Age, occupation, and degreasing chemical exposure also were significant covariates in the Model 3 analysis. When the categorized dioxin-by-race interaction was removed from the final model, the adjusted analysis did not show a significant difference between any of the Ranch Hand categories and the Comparison group (Table 13-36: $p \geq 0.16$ for all analyses).

The unadjusted and adjusted analyses of Models 4 through 6 did not reveal a significant association between serum amylase and current dioxin (Table 13-36(g,h): $p > 0.30$ for all analyses). Each of the adjusted analyses contained age, race, occupation, and degreasing chemical exposure.

Antibodies for Hepatitis A

Neither the unadjusted nor the adjusted Model 1 analyses detected a significant group difference in the percentage of individuals having antibodies for hepatitis A (Table 13-37(a,b): $p > 0.28$ for all contrasts). Age, race, and occupation were significant covariates in the adjusted analysis.

The unadjusted and adjusted Model 2 results did not reveal a significant association between antibodies for hepatitis A and initial dioxin (Table 13-37(c,d): $p > 0.86$ for both analyses). The adjusted model contained age, occupation, and three covariate-by-covariate interactions: race-by-degreasing chemical exposure, race-by-lifetime alcohol history, and industrial chemical exposure-by-lifetime alcohol history.

Neither the unadjusted nor adjusted Model 3 analyses showed any of the Ranch Hand categories to be significantly different from the Comparison group (Table 13-37(e): $p > 0.33$ for all contrasts). The adjusted Model 3 analysis contained occupation and the race-by-age interaction.

Without occupation, the adjusted analysis of Model 3 detected a marginally significant relative risk greater than one for the Ranch Hands in the high category (Appendix Table I-3-27(b): $p = 0.052$, Adj. RR=1.35, 95% C.I.=[1.00, 1.82]) and a marginally significant relative risk less than one for the background Ranch Hands ($p = 0.083$, Adj. RR=0.79, 95% C.I.=[0.61, 1.03]).

Neither the unadjusted nor the adjusted analyses of Models 4 through 6 revealed a significant association between antibodies for hepatitis A and current dioxin (Table 13-37(g,h): $p > 0.15$ for all analyses). Each of the final models contained occupation and two covariate-by-covariate interactions: race-by-age and race-by-lifetime alcohol history.

Excluding occupation from Models 4 through 6 resulted in significant associations between antibodies for hepatitis A and current dioxin (Appendix Table I-3-27(c): $p = 0.002$, Adj. RR=1.18, 95% C.I.=[1.06, 1.32]; $p = 0.002$, Adj. RR=1.15, 95% C.I.=[1.05, 1.26]; and $p = 0.004$, Adj. RR=1.16, 95% C.I.=[1.05, 1.28] for Models 4, 5, and 6 respectively).

Table 13-37.
Analysis of Antibodies for Hepatitis A

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Yes**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***952***	***33.5***	***0.98 (0.82,1.17)***	***0.849***
	Comparison	***1,280***	***34.0***		
Officer	Ranch Hand	367	25.9	1.04 (0.77,1.42)	0.854
	Comparison	502	25.1		
Enlisted Flyer	Ranch Hand	162	47.5	1.13 (0.74,1.71)	0.645
	Comparison	202	44.6		
Enlisted Groundcrew	Ranch Hand	423	34.8	0.87 (0.67,1.13)	0.321
	Comparison	576	38.0		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***0.95 (0.79,1.15)***	***0.634***	AGE (p<0.001) RACE (p=0.021) OCC (p<0.001)
Officer	1.01 (0.73,1.40)	0.937	
Enlisted Flyer	1.11 (0.72,1.72)	0.634	
Enlisted Groundcrew	0.86 (0.65,1.13)	0.283	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 13-37. (Continued)
Analysis of Antibodies for Hepatitis A

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	174	36.2	0.99 (0.86,1.13)	0.864
Medium	173	35.3		
High	173	36.4		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
507	1.00 (0.84,1.18)	0.974	AGE (p<0.001) OCC (p<0.001) RACE*DC (p=0.005) RACE*DRKYR (p<0.001) IC*DRKYR (p=0.009)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 13-37. (Continued)
Analysis of Antibodies for Hepatitis A

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,063	34.1		
Background RH	374	30.5	0.88 (0.68,1.14)	0.338
Low RH	260	35.8	1.04 (0.78,1.38)	0.810
High RH	260	36.2	1.06 (0.80,1.42)	0.667
Low plus High RH	520	36.0	1.05 (0.84,1.31)	0.666

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,063			OCC ($p<0.001$) RACE*AGE ($p=0.037$)
Background RH	374	1.03 (0.78,1.37)	0.827	
Low RH	260	0.91 (0.67,1.24)	0.552	
High RH	260	0.94 (0.69,1.29)	0.720	
Low plus High RH	520	0.93 (0.73,1.18)	0.535	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin $\leq$ 10 ppt.
Background (Ranch Hand): Current Dioxin $\leq$ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin $\leq$ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 13-37. (Continued)
Analysis of Antibodies for Hepatitis A

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Yes/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	30.8 (295)	33.7 (300)	36.5 (299)	1.06 (0.97,1.17)	0.209
5	27.7 (300)	36.4 (297)	37.0 (297)	1.06 (0.98,1.15)	0.152
6[c]	27.4 (299)	36.4 (297)	37.0 (297)	1.05 (0.96,1.15)	0.292

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	874	1.01 (0.90,1.14)	0.818	OCC (p<0.001) RACE*AGE (p=0.014) RACE*DRKYR (p=0.022)
5	874	1.01 (0.92,1.12)	0.782	OCC (p<0.001) RACE*AGE (p=0.014) RACE*DRKYR (p=0.022)
6[d]	873	1.01 (0.90,1.12)	0.897	OCC (p<0.001) RACE*AGE (p=0.016) RACE*DRKYR (p=0.026)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Serological Evidence of Present or Prior Hepatitis B Infection

The unadjusted Model 1 analysis revealed a significant overall group difference in the percentage of individuals with serological evidence of present or prior hepatitis B infection (Table 13-38(a): $p=0.001$, Est. RR=0.66, 95% C.I.=[0.51, 0.85]). The percentage of Ranch Hands with serological evidence of present or prior hepatitis B infection was lower than the percentage for the Comparisons (10.7% vs. 15.5%). Stratifying the unadjusted analysis by occupation revealed a significant group difference within the officer stratum and marginally significant group differences for the enlisted flyer and enlisted groundcrew stratums (Table 13-38(a): $p=0.030$, Est. RR=0.53, 95% C.I.=[0.30, 0.92]; $p=0.077$, Est. RR=0.58, 95% C.I.=[0.33, 1.02]; and $p=0.086$, Est. RR=0.73, 95% C.I.=[0.52, 1.03] respectively). In each occupation stratum, the percentage of participants with serological evidence of present or prior hepatitis B infection was lower for the Ranch Hands than for the Comparisons (5.2% vs. 9.4%, 13.6% vs. 21.3%, and 14.4% vs. 18.8% for the officers, enlisted flyers, and enlisted groundcrew respectively).

After adjusting for the covariates age, race, occupation, and lifetime alcohol history, the adjusted analysis produced results that closely paralleled the unadjusted findings. The adjusted analysis revealed a significant overall group difference (Table 13-38(b): $p<0.001$, Adj. RR=0.65, 95% C.I.=[0.50, 0.84]). When the adjusted results were stratified by occupation, the Model 1 analysis detected a significant group difference for the officers and marginally significant group differences for the enlisted flyers and enlisted groundcrew ($p=0.030$, Adj. RR=0.54, 95% C.I.=[0.31, 0.94]; $p=0.082$, Adj. RR=0.60, 95% C.I.=[0.34, 1.07]; and $p=0.060$, Adj. RR=0.71, 95% C.I.=[0.50, 1.01] respectively).

The unadjusted Model 2 analysis revealed a marginally significant positive association between serological evidence of present or prior hepatitis B infection and initial dioxin (Table 13-38(c): $p=0.054$, Est. RR=1.21, 95% C.I.=[1.00, 1.48]). After covariate adjustment, the Model 2 analysis did not show a significant association between serological evidence of present or prior hepatitis B infection and initial dioxin (Table 13-38(d): $p=0.308$). Age, occupation, and the race-by-lifetime alcohol history interaction were retained in the adjusted analysis.

Without occupation, the adjusted Model 2 analysis generated different results. The analysis revealed a significant positive association between serological evidence of present or prior hepatitis B infection and initial dioxin (Appendix Table I-3-28(a): $p=0.016$, Est. RR=1.31, 95% C.I.=[1.05, 1.63]).

The unadjusted Model 3 analysis revealed three significant contrasts: background Ranch Hands versus Comparisons, low Ranch Hands versus Comparisons, and low plus high Ranch Hands versus Comparisons (Table 13-38(e): $p=0.013$, Est. RR=0.61, 95% C.I.=[0.41, 0.90]; $p=0.030$, Est. RR=0.61, 95% C.I.=[0.40, 0.95]; and $p=0.033$, Est. RR=0.71, 95% C.I.=[0.51, 0.97] respectively). The percentages of participants with serological evidence of present or prior hepatitis B infection for the Comparisons, background Ranch Hands, low Ranch Hands, and low plus high Ranch Hands were 15.1%, 9.4%, 10.0%, and 11.5% respectively.

Table 13-38.
Analysis of Serological Evidence of Present or Prior Hepatitis B Infection

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Percent Yes	Est. Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*952*	*10.7*	*0.66 (0.51,0.85)*	*0.001*
	Comparison	*1,280*	*15.5*		
Officer	Ranch Hand	367	5.2	0.53 (0.30,0.92)	0.030
	Comparison	502	9.4		
Enlisted Flyer	Ranch Hand	162	13.6	0.58 (0.33,1.02)	0.077
	Comparison	202	21.3		
Enlisted Groundcrew	Ranch Hand	423	14.4	0.73 (0.52,1.03)	0.086
	Comparison	576	18.8		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	*0.65 (0.50,0.84)*	*<0.001*	AGE (p=0.003)
Officer	0.54 (0.31,0.94)	0.030	RACE (p<0.001)
Enlisted Flyer	0.60 (0.34,1.07)	0.082	OCC (p<0.001)
Enlisted Groundcrew	0.71 (0.50,1.01)	0.060	DRKYR (p=0.011)

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 13-38. (Continued)
Analysis of Serological Evidence of Present or Prior Hepatitis B Infection

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	174	8.0	1.21 (1.00,1.48)	0.054
Medium	173	9.2		
High	173	17.3		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
507	1.13 (0.89,1.43)	0.308	AGE (p=0.047) OCC (p=0.001) RACE*DRKYR (p<0.001)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 13-38. (Continued)
Analysis of Serological Evidence of Present or Prior Hepatitis B Infection

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,063	15.1		
Background RH	374	9.4	0.61 (0.41,0.90)	0.013
Low RH	260	10.0	0.61 (0.40,0.95)	0.030
High RH	260	13.1	0.80 (0.53,1.19)	0.272
Low plus High RH	520	11.5	0.71 (0.51,0.97)	0.033

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,045			DXCAT*AGE (p=0.044) DXCAT*OCC (p=0.024) RACE (p=0.004) DRKYR (p=0.032)
Background RH	367	0.77 (0.52,1.16)**	0.211**	
Low RH	254	0.58 (0.37,0.92)**	0.020**	
High RH	253	0.65 (0.42,0.98)**	0.041**	
Low plus High RH	507	0.62 (0.44,0.86)**	0.004**	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interactions ($p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table I-2-25 for further analysis of these interactions.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 13-38. (Continued)
Analysis of Serological Evidence of Present or Prior Hepatitis B Infection

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Yes/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	8.8 (295)	9.3 (300)	13.7 (299)	1.13 (0.98,1.30)	0.098
5	9.3 (300)	8.4 (297)	14.1 (297)	1.11 (0.98,1.26)	0.109
6[c]	9.4 (299)	8.4 (297)	14.1 (297)	1.10 (0.96,1.26)	0.152

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	874	0.97 (0.82,1.14)**	0.674**	CURR*OCC (p=0.006) RACE*DRKYR (p=0.001)
5	874	0.97 (0.85,1.11)**	0.677**	CURR*OCC (p=0.011) RACE*DRKYR (p=0.001)
6[d]	873	0.96 (0.82,1.11)**	0.554**	CURR*OCC (p=0.014) RACE*DRKYR (p=0.001)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-25 for further analysis of this interaction.

Note: Model 4: Low = $\leq$ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = $\leq$ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Categorized dioxin-by-age and categorized dioxin-by-occupation were significant covariates in the adjusted analysis (Table 13-38(f): p=0.044 and p=0.024 respectively). The final model also included a race-and-lifetime alcohol history interaction. Appendix Table I-2-25 displays adjusted results stratified separately by age and occupation. After the two categorized dioxin-by-covariate interactions were removed from the final model, the low Ranch Hands versus Comparisons and the low plus high Ranch Hands versus Comparisons contrasts remained significant (Table 13-38(f): p=0.020, Adj. RR=0.58, 95% C.I.=[0.37, 0.92] and p=0.004, Adj. RR=0.62, 95% C.I.=[0.44, 0.86] respectively). In contrast to the unadjusted results, the high Ranch Hands versus Comparisons contrast became significant (13-38(f): p=0.041, Adj. RR=0.65, 95% C.I.=[0.42, 0.98]) and the background Ranch Hands versus Comparisons contrasts became nonsignificant (p=0.211).

The adjusted results corresponded with the unadjusted results after occupation was deleted from the final model, revealing three significant contrasts: background Ranch Hands versus Comparisons, low Ranch Hands versus Comparisons, and low plus high Ranch Hands versus Comparisons (Appendix Table I-3-28(b): p=0.020, Adj. RR=0.63, 95% C.I.=[0.42, 0.93]; p=0.018, Adj. RR=0.58, 95% C.I.=[0.37, 0.91] and p=0.028, Adj. RR=0.69, 95% C.I.=[0.50, 0.96] respectively).

The unadjusted Model 4 analysis detected a marginally significant positive association between serological evidence of present or prior hepatitis B infection and current dioxin (Table 13-38(g): p=0.098, Est. RR=1.13, 95% C.I.=[0.98, 1.30]). The unadjusted Model 5 and 6 analyses did not show a significant association (p>0.10 for both analyses).

Current dioxin-by-occupation was a significant interaction in each of the adjusted analyses for Models 4, 5, and 6 (Table 13-38(h): p=0.006, p=0.011, and p=0.014 respectively). Appendix Table I-2-25 presents adjusted results stratified by occupation for Models 4 through 6. The race-by-lifetime alcohol history interaction also was included in the adjusted analyses. After excluding the current dioxin-by-occupation interaction, the adjusted analyses for Models 4 through 6 did not reveal a significant association between serological evidence of present or prior hepatitis B infection and current dioxin (Table 13-38(h): p>0.55 for all analyses).

Antibodies for Hepatitis C

The unadjusted Model 1 analysis revealed a marginally significant overall group difference in the percentage of participants with antibodies for Hepatitis C (Table 13-39(a): p=0.084, Est. RR=0.46, 95% C.I.=[0.21, 1.04]). The percentage of individuals with antibodies for hepatitis C was lower for the Ranch Hands than for the Comparisons (0.8% vs. 1.8%). The stratified occupation analysis did not generate an estimated relative risk for the enlisted flyer stratum because none of the enlisted flyer Ranch Hands had antibodies for hepatitis C.

The adjusted Model 1 analysis detected significant interactions between group and age (Table 13-39(b): p=0.003) and between group and degreasing chemical exposure (p=0.040). Race also was retained in the final model. Appendix Table I-2-26 presents results stratified separately for age and degreasing chemical exposure. The adjusted relative risk for the

Table 13-39.
Analysis of Antibodies for Hepatitis C

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Yes**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	*Ranch Hand*	*952*	*0.8*	*0.46 (0.21,1.04)*	*0.084*
	Comparison	*1,280*	*1.8*		
Officer	Ranch Hand	367	0.8	0.58 (0.15,2.27)	0.641
	Comparison	502	1.4		
Enlisted Flyer	Ranch Hand	162	0.0	--	--
	Comparison	202	2.0		
Enlisted Groundcrew	Ranch Hand	423	1.2	0.56 (0.20,1.61)	0.400
	Comparison	576	2.1		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	*0.46 (0.21,1.03)***	*0.048***	GROUP*AGE (p=0.003)
Officer	0.60 (0.15,2.33)**	0.457**	GROUP*DC (p=0.040) RACE (p=0.039)
Enlisted Flyer	--	--	
Enlisted Groundcrew	0.55 (0.19,1.59)**	0.272**	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

** Group-by-covariate interactions ($p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table I-2-26 for further analysis of these interactions.

--: Adjusted relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities.

Table 13-39. (Continued)
Analysis of Antibodies for Hepatitis C

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	174	0.6	0.42 (0.08,2.18)	0.229
Medium	173	0.6		
High	173	0.0		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
520	0.97 (0.14,6.98)	0.979	AGE (p=0.016) RACE (p=0.001)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 13-39. (Continued)
Analysis of Antibodies for Hepatitis C

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Percent Yes	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,063	1.5		
Background RH	374	0.5	0.31 (0.07,1.37)	0.122
Low RH	260	0.4	0.27 (0.04,2.06)	0.207
High RH	260	0.4	0.28 (0.04,2.11)	0.215
Low plus High RH	520	0.4	0.27 (0.06,1.20)	0.086

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,063			DC (p=0.066) RACE*AGE (p=0.002)
Background RH	374	0.33 (0.08,1.49)	0.151	
Low RH	260	0.17 (0.02,1.46)	0.107	
High RH	260	0.27 (0.04,2.11)	0.212	
Low plus High RH	520	0.21 (0.05,0.99)	0.048	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 13-39. (Continued)
Analysis of Antibodies for Hepatitis C

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Yes/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	0.7 (295)	0.3 (300)	0.3 (299)	0.73 (0.35,1.53)	0.394
5	1.0 (300)	0.0 (297)	0.3 (297)	0.73 (0.44,1.21)	0.245
6[c]	1.0 (299)	0.0 (297)	0.3 (297)	0.89 (0.47,1.70)	0.727

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	894	0.65 (0.30,1.39)	0.252	AGE (p=0.071) RACE (p=0.023)
5	894	0.65 (0.38,1.13)	0.154	AGE (p=0.070) RACE (p=0.022)
6[d]	893	0.78 (0.42,1.47)	0.461	AGE (p=0.060) RACE (p=0.022)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

overall group contrast became significantly less than one when the two group-by-covariate interactions were removed from the final model (Table 13-39(b): $p=0.048$, Adj. $RR=0.46$, 95% C.I.=[0.21, 1.03]). The adjusted relative risks stratified by occupation were less than one, but not significant.

The unadjusted and adjusted Model 2 analyses did not detect a significant association between antibodies for hepatitis C and initial dioxin (Table 13-39(c,d): $p>0.22$ for both analyses). The adjusted analysis contained age and race.

The unadjusted Model 3 results revealed a marginally significant difference between the low plus high Ranch Hands and Comparisons in the percentage of individuals with antibodies for hepatitis C (Table 13-39(e): $p=0.086$, Est. $RR=0.27$, 95% C.I.=[0.06, 1.20]). The percentages of participants with antibodies for hepatitis C for the Comparisons and low plus high Ranch Hands were 1.5 percent and 0.4 percent respectively.

After adjusting for degreasing chemical exposure and the race-by-age interaction in the Model 3 analysis, the contrasts between the low plus high Ranch Hands and Comparisons became significant (Table 13-39(f): $p=0.048$, Adj. $RR=0.21$, 95% C.I.=[0.05, 0.99]).

The unadjusted and adjusted analyses for Models 4 through 6 did not reveal a significant association between antibodies for hepatitis C and current dioxin (Table 13-39(g,h): $p>0.15$ for all analyses). Each of the adjusted analyses contained age and race.

Stool Hemoccult

The unadjusted Model 1 analysis did not reveal a significant group difference in the percentage of individuals with blood in their stools (Table 13-40(a): $p>0.39$ for all contrasts).

The stratified occupation analysis could not produce an estimated relative risk for the enlisted flyer stratum because stool blood was not detected in any of the enlisted flyer Ranch Hands.

The group-by-lifetime alcohol history interaction was significant in the adjusted Model 1 analysis (Table 13-40(b): $p=0.030$). Occupation and the current alcohol use-by-industrial chemical exposure interaction also were significant in the final model. Appendix Table I-2-27 displays adjusted results stratified by lifetime alcohol history. After the group-by-lifetime alcohol history interaction was removed from the final model, no significant group contrasts were found in the adjusted analysis ($p>0.33$ for all contrasts).

The unadjusted and adjusted Model 2 analyses did not detect a significant association between stool hemoccult results and initial dioxin (Table 13-40(c,d): $p>0.31$ for both analyses). Occupation was the only significant covariate in the adjusted analysis.

The unadjusted Model 3 results revealed a significant difference between the low Ranch Hands and Comparisons in the percentage of participants with positive stool hemoccult tests (Table 13-40(e): $p=0.031$, Est. $RR=2.39$, 95% C.I.=[1.08, 5.27]). The low Ranch Hands

Table 13-40.
Analysis of Stool Hemoccult

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Yes**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	*Ranch Hand*	*898*	*2.6*	*1.35 (0.75,2.41)*	*0.397*
	Comparison	*1,200*	*1.9*		
Officer	Ranch Hand	352	2.6	1.54 (0.59,4.04)	0.522
	Comparison	478	1.7		
Enlisted Flyer	Ranch Hand	152	0.0	--	--
	Comparison	192	1.0		
Enlisted Groundcrew	Ranch Hand	394	3.6	1.47 (0.68,3.15)	0.433
	Comparison	530	2.5		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	*1.35 (0.74,2.45)***	*0.332***	GROUP*DRKYR (p=0.030)
Officer	1.59 (0.61,4.18)**	0.346**	OCC (p=0.024) ALC*IC (p<0.001)
Enlisted Flyer	--	--	
Enlisted Groundcrew	1.42 (0.64,3.13)**	0.384**	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

** Group-by-covariate interaction ($p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-27 for further analysis of this interaction.

Table 13-40. (Continued)
Analysis of Stool Hemoccult

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	166	2.4	0.80 (0.51,1.26)	0.313
Medium	161	4.3		
High	163	1.8		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
490	0.83 (0.50,1.36)	0.449	OCC (p=0.033)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 13-40. (Continued)
Analysis of Stool Hemoccult

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	**n**	**Percent Yes**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,005	1.8		
Background RH	358	1.7	0.93 (0.36,2.39)	0.885
Low RH	247	4.0	2.39 (1.08,5.27)	0.031
High RH	243	1.6	0.89 (0.30,2.68)	0.841
Low plus High RH	490	2.9	1.62 (0.79,3.30)	0.184

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	**n**	**Adj. Relative Risk (95% C.I.)[ac]**	**p-Value**	**Covariate Remarks**
Comparison	987			OCC (p=0.010) RACE*DRKYR (p=0.013) IC*ALC (p<0.001) DC*DRKYR (p=0.043)
Background RH	351	0.80 (0.30,2.14)	0.657	
Low RH	241	2.49 (1.06,5.85)	0.037	
High RH	236	1.14 (0.35,3.68)	0.825	
Low plus High RH	477	1.87 (0.87,4.02)	0.110	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 13-40. (Continued)
Analysis of Stool Hemoccult

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[a]	Current Dioxin Category Percent Yes/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) Est. Relative Risk (95% C.I.)[b]	p-Value
4	1.8 (282)	2.8 (288)	2.5 (278)	1.05 (0.77,1.41)	0.774
5	1.7 (287)	2.8 (284)	2.5 (277)	1.09 (0.84,1.42)	0.522
6[c]	1.7 (286)	2.8 (284)	2.5 (277)	1.01 (0.76,1.34)	0.962

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[a]	n	Analysis Results for Log_2 (Current Dioxin + 1) Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	828	1.12 (0.77,1.62)	0.554	OCC (p=0.020) DRKYR (p=0.032) RACE*ALC (p=0.013) IC*ALC (p=0.014)
5	828	1.15 (0.83,1.60)	0.379	OCC (p=0.018) DRKYR (p=0.031) RACE*ALC (p=0.013) IC*ALC (p=0.013)
6[d]	827	1.09 (0.77,1.55)	0.631	OCC (p=0.022) DRKYR (p=0.035) RACE*ALC (p=0.018) IC*ALC (p=0.017)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

were more than twice as likely as Comparisons to have positive stool hemoccult tests (Table 13-40(e): 4.0% vs. 1.8%).

After adjusting for covariates in the Model 3 analysis, the contrast between the low Ranch Hands and Comparisons remained significant (Table 13-40(f): p=0.037, Adj. RR=2.49, 95% C.I.=[1.06, 5.85]). The final model contained occupation and three interactions: race-by-lifetime alcohol history, industrial chemical exposure-by-current alcohol use, and degreasing chemical exposure-by-lifetime alcohol history.

The unadjusted and adjusted analyses for Models 4 through 6 did not reveal a significant association between positive stool hemoccult and current dioxin (Table 13-40(g,h): p>0.37 for all analyses). Each of the final models contained occupation, lifetime alcohol history, and two interactions: race-by-current alcohol use and industrial chemical exposure-by-current alcohol use.

Prealbumin (Continuous)

The unadjusted Model 1 analysis did not disclose a significant group difference in the mean levels of prealbumin (Table 13-41(a): p>0.76 for all contrasts). The interaction between group and current alcohol use was significant in the adjusted Model 1 analysis (Table 13-41(b): p=0.022). Occupation and the age-by-lifetime alcohol history interaction also were significant in the final model. Appendix Table I-2-28 presents adjusted results stratified by current alcohol use. The adjusted Model 1 analysis did not show a significant group difference in the mean levels of prealbumin when the group-by-current alcohol use interaction was removed from the final model (Table 13-41(b): p>0.76 for all contrasts).

Examination of the unadjusted Model 2 results did not show a significant association between prealbumin and initial dioxin (Table 13-41(c): p=0.961). The initial dioxin-by-industrial chemical exposure interaction was significant in the adjusted Model 2 analysis (Table 13-41(d): p=0.013). Appendix Table I-2-28 displays adjusted results stratified by industrial chemical exposure. Age and current alcohol use also were significant covariates in the adjusted analysis. After the initial dioxin-by-industrial chemical interaction was removed from the final model, the adjusted analysis did not show a significant association between prealbumin and initial dioxin (Table 13-41(d): p=0.524).

The unadjusted Model 3 results did not show any of the Ranch Hand categories to be significantly different from the Comparison group in the mean levels of prealbumin (Table 13-41(e): p>0.64 for each contrast). Categorized dioxin-by-industrial chemical exposure was a significant interaction in the adjusted Model 3 analysis (Table 13-41(f): p=0.009). Appendix Table I-2-28 displays adjusted results stratified by industrial chemical exposure. Occupation, current alcohol use, and the age-by-lifetime alcohol history interaction also were significant in the final model. The adjusted Model 3 analysis did not uncover a significant difference between any of the Ranch Hand categories and the Comparison group after removing the categorized dioxin-by-industrial chemical exposure interaction from the final model (Table 13-41(f): p>0.53 for all contrasts).

Table 13-41.
Analysis of Prealbumin (mg/dl)
(Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Mean**	**Difference of Means (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***939***	***27.72***	***-0.01 (-0.38,0.37)***	***0.975***
	Comparison	***1,253***	***27.73***		
Officer	Ranch Hand	361	27.95	0.09 (-0.53,0.72)	0.767
	Comparison	495	27.85		
Enlisted Flyer	Ranch Hand	162	27.64	-0.03 (-0.90,0.84)	0.943
	Comparison	196	27.67		
Enlisted Groundcrew	Ranch Hand	416	27.56	-0.08 (-0.64,0.48)	0.782
	Comparison	562	27.64		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED						
Occupational Category	**Group**	**n**	**Adj. Mean**	**Difference of Adj. Means (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***Ranch Hand***	***917***	***27.80*****	***0.05 (-0.32,0.42)*****	***0.788*****	GROUP*ALC (p=0.022)
	Comparison	***1,232***	***27.75*****			OCC (p<0.001)
Officer	Ranch Hand	357	28.23**	0.09 (-0.51,0.68)**	0.777**	AGE*DRKYR (p=0.045)
	Comparison	487	28.14**			
Enlisted Flyer	Ranch Hand	156	27.92**	0.14 (-0.78,1.06)**	0.765**	
	Comparison	195	27.78**			
Enlisted Groundcrew	Ranch Hand	404	27.28**	-0.01 (-0.57,0.55)**	0.964**	
	Comparison	550	27.29**			

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

** Group-by-covariate interaction (0.01<p≤0.05); adjusted mean, difference of adjusted means, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-28 for further analysis of this interaction.

Table 13-41. (Continued)
Analysis of Prealbumin (mg/dl)
(Continuous)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[a]		
Initial Dioxin	n	Mean	Adj. Mean[a]	R^2	Slope (Std. Error)	p-Value
Low	173	27.70	27.65	0.034	-0.0073 (0.1474)	0.961
Medium	170	27.40	27.34			
High	172	27.72	27.83			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[b]			
Initial Dioxin	n	Adj. Mean[b]	R^2	Adj. Slope (Std. Error)	p-Value	Covariate Remarks
Low	171	27.81**	0.077	-0.0977 (0.1530)**	0.524**	INIT*IC (p=0.013) AGE (p=0.020) ALC (p=0.001)
Medium	167	27.43**				
High	170	27.70**				

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-28 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 13-41. (Continued)
Analysis of Prealbumin (mg/dl)
(Continuous)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED					
Dioxin Category	**n**	**Mean**	**Adj. Mean**[a]	**Difference of Adj. Mean vs. Comparisons (95% C.I.)**	**p-Value**
Comparison	1,043	27.71	27.72		
Background RH	369	27.80	27.59	-0.13 (-0.66,0.41)	0.642
Low RH	257	27.53	27.65	-0.07 (-0.68,0.54)	0.828
High RH	258	27.68	27.84	0.12 (-0.49,0.73)	0.691
Low plus High RH	515	27.61	27.75	0.03 (-0.44,0.50)	0.908

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED					
Dioxin Category	**n**	**Adj. Mean**[b]	**Difference of Adj. Mean vs. Comparisons (95% C.I.)**	**p-Value**	**Covariate Remarks**
Comparison	1,025	27.75**			DXCAT*IC (p=0.009) OCC (p=0.012) ALC (p<0.001) AGE*DRKYR (p=0.013)
Background RH	362	27.58**	-0.17 (-0.71,0.37)**	0.537**	
Low RH	251	27.82**	0.07 (-0.54,0.67)**	0.827**	
High RH	251	27.93**	0.17 (-0.45,0.80)**	0.589**	
Low plus High RH	502	27.87**	0.12 (-0.35,0.59)**	0.620**	

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interaction ($p \leq 0.05$); adjusted mean, difference of adjusted means, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-28 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 13-41. (Continued)
Analysis of Prealbumin (mg/dl)
(Continuous)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED						
	Current Dioxin Category Mean/(n)			Analysis Results for Log_2 (Current Dioxin + 1)		
Model[a]	Low	Medium	High	R^2	Slope (Std. Error)	p-Value
4	28.05 (290)	27.50 (298)	27.52 (296)	<0.001	-0.0193 (0.1040)	0.853
5	27.74 (294)	27.68 (297)	27.65 (293)	0.001	0.0977 (0.0893)	0.274
6[b]	28.12 (293)	27.71 (297)	27.27 (293)	0.029	-0.0968 (0.0947)	0.307

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED							
	Current Dioxin Category Adjusted Mean/(n)			Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	Low	Medium	High	R^2	Adj. Slope (Std. Error)	p-Value	Covariate Remarks
4	28.10** (287)	27.68** (290)	27.61** (287)	0.055	-0.0277 (0.1080)**	0.798**	CURR*DC (p=0.002) CURR*IC (p=0.027) ALC (p<0.001) DRKYR (p=0.075) AGE*DC (p=0.018)
5	27.76** (290)	27.84** (290)	27.91** (284)	0.065	0.1569 (0.0994)**	0.115**	CURR*DC (p<0.001) CURR*OCC (p=0.007) ALC (p<0.001) DRKYR (p=0.098) AGE*DC (p=0.010)
6[c]	28.20** (289)	27.88** (290)	27.36** (284)	0.087	-0.1088 (0.0978)**	0.266**	CURR*DC (p=0.001) CURR*IC (p=0.008) ALC (p<0.001) DRKYR (p=0.042) AGE*DC (p=0.020)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Adjusted for log_2 total lipids.

[c] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($p \leq 0.05$); adjusted mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-28 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

The unadjusted analyses for Models 4 through 6 did not detect a significant association between prealbumin and current dioxin (Table 13-41(g): $p>0.27$ for all analyses). Current dioxin-by-degreasing chemical exposure and current dioxin-by-industrial chemical exposure were significant covariates in each of the adjusted analyses for Models 4 through 6 (Table 13-41(h): $p=0.002$ and $p=0.027$; $p<0.001$ and $p=0.007$; $p=0.001$ and $p=0.008$ respectively). Appendix Table I-2-28 presents adjusted results stratified separately by degreasing chemical exposure and industrial chemical exposure for Models 4 through 6. Each of the final models also contained current alcohol use, lifetime alcohol history, and the age-by-degreasing chemical exposure interaction. When the two current dioxin-by-covariate interactions were removed from each of the final models, none of the adjusted analyses for Models 4 through 6 found prealbumin to be significantly associated with current dioxin (Table 13-41(h): $p>0.11$ for all analyses).

Prealbumin (Discrete)

The unadjusted and adjusted Model 1 analyses did not show a significant group difference in the percentage of participants with low levels of prealbumin (Table 13-42(a,b): $p>0.26$ for all contrasts). The adjusted model contained the covariates age and current alcohol use.

The unadjusted Model 2 analysis did not find a significant association between prealbumin and initial dioxin (Table 13-42(c): $p=0.282$). The adjusted Model 2 results were identical to the unadjusted results because no covariates were retained in the final model.

Examination of the unadjusted and adjusted Model 3 results did not show any of the Ranch Hand categories to be significantly different from the Comparison group (Table 13-42(e,f): $p>0.16$ for all contrasts). The final model contained age and current alcohol use.

The unadjusted analyses for Models 4 through 6 did not detect a significant association between prealbumin and current dioxin (Table 13-42(g): $p>0.14$ for all analyses). Current dioxin-by-occupation was a significant interaction in the adjusted analyses of Models 4 and 5 (Table 13-42(h): $p=0.002$ for both models). Current dioxin-by-age was a significant interaction in the adjusted Model 6 analysis (Table 13-42(h): $p=0.006$). Appendix Table I-2-29 displays adjusted results stratified by occupation for Models 4 and 5 and also includes adjusted results stratified by age for Model 6. After removing the current dioxin-by-covariate interaction from each of the final models, none of the adjusted analyses for Models 4 through 6 uncovered a significant association between prealbumin and current dioxin (Table 13-42(h): $p>0.10$ for all analyses).

Albumin (Continuous)

The unadjusted Model 1 analysis did not reveal a significant difference between the Ranch Hands and Comparisons in the mean levels of albumin (Table 13-43: $p>0.21$ for all contrasts). Group-by-lifetime alcohol history and group-by-age were significant covariates in the adjusted Model 1 analysis (Table 13-43(b): $p=0.036$ and $p=0.039$ respectively).

Table 13-42.
Analysis of Prealbumin
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Low**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	*Ranch Hand*	*939*	*1.3*	*1.00 (0.47,2.13)*	*0.999*
	Comparison	*1,253*	*1.3*		
Officer	Ranch Hand	361	1.1	0.54 (0.17,1.75)	0.444
	Comparison	495	2.0		
Enlisted Flyer	Ranch Hand	162	1.2	1.21 (0.17,8.70)	0.999
	Comparison	196	1.0		
Enlisted Groundcrew	Ranch Hand	416	1.4	2.04 (0.57,7.28)	0.423
	Comparison	562	0.7		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	*0.97 (0.44,2.13)*	*0.938*	AGE ($p<0.001$) ALC ($p=0.002$)
Officer	0.51 (0.16,1.66)	0.265	
Enlisted Flyer	1.55 (0.21,11.58)	0.670	
Enlisted Groundcrew	2.07 (0.52,8.20)	0.301	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 13-42. (Continued)
Analysis of Prealbumin
(Discrete)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Low	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	173	0.0	1.38 (0.77,2.49)	0.282
Medium	170	1.2		
High	172	1.7		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[a]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
515	1.38 (0.77,2.49)	0.282	

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 13-42. (Continued)
Analysis of Prealbumin
(Discrete)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	**n**	**Percent Low**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,043	1.3		
Background RH	369	1.6	1.39 (0.52,3.69)	0.510
Low RH	257	0.8	0.49 (0.11,2.19)	0.352
High RH	258	1.2	0.70 (0.19,2.55)	0.590
Low plus High RH	515	1.0	0.60 (0.21,1.70)	0.335

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	**n**	**Adj. Relative Risk (95% C.I.)[ac]**	**p-Value**	**Covariate Remarks**
Comparison	1,027			AGE (p=0.017) ALC (p=0.057)
Background RH	367	1.35 (0.50,3.62)	0.555	
Low RH	254	0.23 (0.03,1.84)	0.168	
High RH	254	0.90 (0.24,3.34)	0.879	
Low plus High RH	508	0.52 (0.17,1.65)	0.268	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 13-42. (Continued)
Analysis of Prealbumin
(Discrete)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Low/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	1.4 (290)	1.0 (298)	1.4 (296)	0.87 (0.57,1.33)	0.514
5	1.4 (294)	1.0 (297)	1.4 (293)	0.78 (0.56,1.08)	0.147
6[c]	1.0 (293)	1.0 (297)	1.4 (293)	0.97 (0.65,1.44)	0.882

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	884	0.83 (0.52,1.31)**	0.417**	CURR*OCC (p=0.002)
5	884	0.75 (0.54,1.04)**	0.104**	CURR*OCC (p=0.002)
6[d]	883	1.00 (0.66,1.52)**	0.984**	CURR*AGE (p=0.006)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-29 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 13-43.
Analysis of Albumin (mg/dl)
(Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Mean**	**Difference of Means (95% C.I.)**	**p-Value**
All	*Ranch Hand*	*939*	*3,938.63*	*-15.40 (-41.48,10.68)*	*0.247*
	Comparison	*1,253*	*3,954.03*		
Officer	Ranch Hand	361	3,929.45	-25.79 (-66.52,14.95)	0.215
	Comparison	495	3,955.23		
Enlisted Flyer	Ranch Hand	162	3,926.56	-12.15 (-74.19,49.89)	0.701
	Comparison	196	3,937.70		
Enlisted Groundcrew	Ranch Hand	416	3,951.68	-6.98 (-47.42,33.45)	0.735
	Comparison	562	3,958.67		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED						
Occupational Category	**Group**	**n**	**Adj. Mean**	**Difference of Adj. Means (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	*Ranch Hand*	*917*	*3,910.13***	*-12.15 (-38.06,13.77)*	*0.358***	GROUP*DRKYR (p=0.036)
	Comparison	*1,232*	*3,922.27***			GROUP*AGE (p=0.039)
Officer	Ranch Hand	357	3,919.44**	-23.11 (-64.59,18.37)	0.275**	RACE (p=0.004)
	Comparison	487	3,942.55**			DC (p=0.042)
Enlisted Flyer	Ranch Hand	156	3,916.15**	-2.98 (-66.92,60.95)	0.927**	AGE*IC (p=0.002)
	Comparison	195	3,919.14**			
Enlisted Groundcrew	Ranch Hand	404	3,904.03**	-5.45 (-44.42,33.53)	0.784**	
	Comparison	550	3,909.48**			

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

** Group-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted mean, difference of adjusted means, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-30 for further analysis of this interaction.

Table 13-43. (Continued)
Analysis of Albumin (mg/dl)
(Continuous)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[a]		
Initial Dioxin	n	Mean	Adj. Mean[a]	R^2	Slope (Std. Error)	p-Value
Low	173	3,933.12	3,926.85	0.043	15.9199 (10.1567)	0.118
Medium	170	3,918.12	3,913.79			
High	172	3,971.22	3,981.81			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[b]			
Initial Dioxin	n	Adj. Mean[b]	R^2	Adj. Slope (Std. Error)	p-Value	Covariate Remarks
Low	173	3,878.39**	0.071	8.1440 (10.6839)**	0.446**	INIT*IC (p=0.013) AGE (p=0.104) RACE (p=0.014)
Medium	170	3,852.43**				
High	172	3,909.67**				

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-30 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 13-43. (Continued)
Analysis of Albumin (mg/dl)
(Continuous)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED					
Dioxin Category	**n**	**Mean**	**Adj. Mean[a]**	**Difference of Adj. Mean vs. Comparisons (95% C.I.)**	**p-Value**
Comparison	1,043	3,949	3,949.03		
Background RH	369	3,938	3,921.21	-27.83 (-63.85,8.20)	0.130
Low RH	257	3,913	3,922.34	-26.70 (-67.83,14.44)	0.203
High RH	258	3,968	3,982.08	33.04 (-8.13,74.20)	0.116
Low plus High RH	515	3,941	3,952.21	3.17 (-28.71,35.05)	0.846

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED					
Dioxin Category	**n**	**Adj. Mean[b]**	**Difference of Adj. Mean vs. Comparisons (95% C.I.)**	**p-Value**	**Covariate Remarks**
Comparison	1,027	3,936.55**			DXCAT*IC (p=0.020) ALC (p=0.108) AGE*IC (p=0.001) OCC*IC (p=0.041) OCC*RACE (p=0.048)
Background RH	367	3,916.86**	-19.68 (-56.12,16.75)**	0.290**	
Low RH	254	3,921.28**	-15.27 (-56.22,25.69)**	0.465**	
High RH	254	3,962.35**	25.80 (-16.50,68.11)**	0.232**	
Low plus High RH	508	3,941.82**	5.27 (26.79,37.33)**	0.747**	

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted mean, difference of adjusted means, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-30 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 13-43. (Continued)
Analysis of Albumin (mg/dl)
(Continuous)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED						
	Current Dioxin Category Mean/(n)			Analysis Results for Log_2 (Current Dioxin + 1)		
Model[a]	Low	Medium	High	R^2	Slope (Std. Error)	p-Value
4	3,956.28 (290)	3,901.34 (298)	3,962.43 (296)	<0.001	2.7200 (6.9959)	0.698
5	3,950.34 (294)	3,909.97 (297)	3,959.52 (293)	0.001	4.4671 (6.0070)	0.457
6[b]	3,958.44 (293)	3,910.73 (297)	3,950.89 (293)	0.004	0.4077 (6.4688)	0.950

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED							
	Current Dioxin Category Adjusted Mean/(n)			Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	Low	Medium	High	R^2	Adj. Slope (Std. Error)	p-Value	Covariate Remarks
4	3,929.48** (289)	3,880.46** (295)	3,923.76** (291)	0.047	-3.4551 (8.0212)**	0.667**	CURR*ALC (p=0.006) CURR*DC (p=0.011) RACE (p=0.034) AGE*IC (p=0.020) ALC*OCC (p=0.010)
5	3,924.57** (292)	3,888.18** (295)	3,920.81** (288)	0.047	0.3387 (6.7815)**	0.960**	CURR*ALC (p=0.008) CURR*DC (p=0.016) RACE (p=0.043) AGE*IC (p=0.023) ALC*OCC (p=0.012)
6[c]	3,937.34** (291)	3,892.30** (295)	3,912.69** (288)	0.051	-4.8440 (7.3150)**	0.508**	CURR*ALC (p=0.009) CURR*DC (p=0.016) RACE (p=0.057) AGE*IC (p=0.027) ALC*OCC (p=0.012)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Adjusted for log_2 total lipids.

[c] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($p \leq 0.05$); adjusted mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-30 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Appendix Table I-2-30 presents adjusted results stratified separately by age and lifetime alcohol history. The final adjusted model also included race, degreasing chemical exposure, and the age-by-industrial chemical exposure interaction. After the two group-by-covariate interactions were removed from the final model, the adjusted Model 1 analysis did not detect any significant group contrasts (Table 13-43(b): $p>0.27$ for each contrast).

The unadjusted Model 2 results did not show a significant association between albumin and initial dioxin (Table 13-43(c): $p=0.118$). The adjusted Model 2 analysis contained a significant interaction between initial dioxin and industrial chemical exposure (Table 13-43(d): $p=0.013$). Appendix Table I-2-30 presents adjusted results stratified by industrial chemical exposure. In addition to the initial dioxin-by-industrial chemical exposure interaction, the final adjusted model also included age and race. The adjusted Model 2 analysis did not reveal a significant association between albumin and initial dioxin when the initial dioxin-by-industrial chemical exposure interaction was removed from the final model (Table 13-43(d): $p=0.446$).

The unadjusted Model 3 analysis did not reveal a significant difference between any of the Ranch Hand categories and the Comparison group in the mean levels of albumin (Table 13-43(e): $p>0.11$ for all contrasts). Categorized dioxin-by-industrial chemical exposure was a significant interaction in the adjusted Model 3 analysis (Table 13-43(f): $p=0.020$). Appendix Table I-2-30 displays adjusted results stratified by industrial chemical exposure. In addition to this interaction, the adjusted analysis also contained current alcohol use and three significant covariate-by-covariate interactions: age-by-industrial chemical exposure, occupation-by-industrial chemical exposure, and occupation-by-race. The adjusted Model 3 analysis did not show any of the Ranch Hand categories to be significantly different from the Comparison group when categorized dioxin-by-industrial chemical exposure was removed from the final model (Table 13-43(f): $p>0.23$ for all contrasts).

The unadjusted analyses for Models 4 through 6 did not reveal a significant association between albumin and current dioxin (Table 13-43(g): $p>0.45$ for all analyses). Current dioxin-by-current alcohol and current dioxin-by-degreasing chemical exposure were significant covariates in each of the adjusted analyses of Models 4 through 6 (Table 13-43(h): $p=0.006$ and $p=0.011$; $p=0.008$ and $p=0.016$; $p=0.009$ and $p=0.016$ respectively). Appendix Table I-2-30 displays adjusted results stratified separately by current alcohol use and degreasing chemical exposure for Models 4 through 6. Each of the adjusted analyses also included race and two significant covariate-by-covariate interactions: age-by-industrial chemical exposure and current alcohol use-by-occupation. After removing the current dioxin-by-covariate interactions from each of the final models, none of the adjusted analyses for Models 4 through 6 showed albumin to be significantly associated with current dioxin (Table 13-43(h): $p>0.50$).

Albumin (Discrete)

The unadjusted Model 1 analysis did not reveal a significant group difference in the percentage of individuals with low albumin levels (Table 13-44(a): $p>0.50$ for all contrasts). The interaction between group and industrial chemical exposure was significant in the adjusted Model 1 analysis. Appendix Table I-2-31 presents adjusted results stratified by

Table 13-44.
Analysis of Albumin
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	Group	n	Percent Low	Est. Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*939*	*2.4*	*1.10 (0.63,1.92)*	*0.852*
	Comparison	*1,253*	*2.2*		
Officer	Ranch Hand	361	2.2	1.58 (0.57,4.40)	0.536
	Comparison	495	1.4		
Enlisted Flyer	Ranch Hand	162	1.9	0.51 (0.13,2.00)	0.509
	Comparison	196	3.6		
Enlisted Groundcrew	Ranch Hand	416	2.9	1.16 (0.53,2.54)	0.859
	Comparison	562	2.5		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	*1.08 (0.61,1.89)***	*0.794***	GROUP*IC (p=0.029) OCC (p=0.104) AGE*IC (p=0.018)
Officer	1.61 (0.57,4.50)**	0.366**	
Enlisted Flyer	0.50 (0.13,1.95)**	0.316**	
Enlisted Groundcrew	1.13 (0.51,2.49)**	0.756**	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

** Group-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-31 for further analysis of this interaction.

Table 13-44. (Continued)
Analysis of Albumin
(Discrete)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Low	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	173	1.7	1.11 (0.76,1.62)	0.599
Medium	170	2.9		
High	172	2.9		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[a]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
515	1.11 (0.76,1.62)	0.599	

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 13-44. (Continued)
Analysis of Albumin
(Discrete)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	**n**	**Percent Low**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,043	2.3		
Background RH	369	2.4	1.26 (0.58,2.77)	0.559
Low RH	257	2.7	1.05 (0.44,2.48)	0.917
High RH	258	2.3	0.86 (0.34,2.15)	0.743
Low plus High RH	515	2.5	0.95 (0.47,1.90)	0.887

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	**n**	**Adj. Relative Risk (95% C.I.)[ab]**	**p-Value**	**Covariate Remarks**
Comparison	1,043			
Background RH	369	1.26 (0.58,2.77)	0.559	
Low RH	257	1.05 (0.44,2.48)	0.917	
High RH	258	0.86 (0.34,2.15)	0.743	
Low plus High RH	515	0.95 (0.47,1.90)	0.887	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

Note: RH = Ranch Hand.
Comparison: Current Dioxin $\leq$ 10 ppt.
Background (Ranch Hand): Current Dioxin $\leq$ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin $\leq$ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 13-44. (Continued)
Analysis of Albumin
(Discrete)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Low/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	1.7 (290)	3.0 (298)	2.7 (296)	1.13 (0.86,1.50)	0.387
5	1.7 (294)	2.7 (297)	3.1 (293)	1.08 (0.84,1.39)	0.529
6[c]	1.7 (293)	2.7 (297)	3.1 (293)	1.09 (0.84,1.43)	0.516

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	884	1.13 (0.86,1.49)	0.393	RACE (p=0.116)
5	884	1.08 (0.84,1.38)	0.541	RACE (p=0.116)
6[d]	883	1.09 (0.84,1.42)	0.510	RACE (p=0.113)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

industrial chemical exposure. Occupation and the age-by-industrial chemical exposure interaction also were significant in the final model. After the group-by-industrial chemical exposure interaction was removed from the final model, the adjusted Model 1 analysis did not show any significant group contrasts (Table 13-44(b): $p>0.31$).

The unadjusted Model 2 analysis did not reveal a significant association between albumin and initial dioxin (Table 13-44(c): $p=0.599$). The unadjusted and adjusted results were identical because no covariates were retained in the adjusted Model 2 analysis. Model 3 analysis results did not show any of the Ranch Hand categories to be significantly different from the Comparison group in the percentage of participants with low albumin levels (Table 13-44(e): $p>0.55$ for all contrasts). The adjusted results were identical to the unadjusted findings because no covariates were retained in the final model.

The unadjusted and adjusted analyses for Models 4 through 6 did not detect a significant association between albumin and current dioxin (Table 13-44(g,h): $p>0.38$ for all analyses). Race was the only covariate in each of the adjusted analyses.

α-1 Acid Glycoprotein (Continuous)

The unadjusted and adjusted Model 1 analyses did not reveal a significant group difference in the mean levels of α-1 acid glycoprotein (Table 13-45(a): $p>0.25$ for all contrasts). The adjusted Model 1 analysis contained race, occupation, and two interactions: lifetime alcohol history-by-current alcohol use and age-by-current alcohol use.

The unadjusted Model 2 analysis did not reveal a significant association between α-1 acid glycoprotein and initial dioxin (Table 13-45(c): $p=0.745$). Initial dioxin-by-lifetime alcohol history and initial dioxin-by-occupation were significant interactions in the adjusted Model 2 analysis (Table 13-45(d): $p=0.007$ and $p=0.022$ respectively). Appendix Table I-2-32 presents adjusted results stratified separately by occupation and lifetime alcohol history. In addition to the two initial dioxin-by-covariate interactions, race and the occupation-by-industrial chemical exposure interaction also were significant in the final model. In contrast to the unadjusted results, the adjusted Model 2 analysis revealed a marginally significant inverse association between α-1 acid glycoprotein and initial dioxin when the two initial dioxin-by-covariate interactions were removed from the final model (Table 13-45(d): $p=0.097$, Adj. Slope=-0.0134).

Removing occupation from the final Model 2 analysis changed the adjusted results. Without occupation and the initial dioxin-by-lifetime alcohol history interaction, the adjusted Model 2 analysis did not find a significant association between α-1 acid glycoprotein and initial dioxin (Appendix Table I-3-32(a): $p=0.898$).

The unadjusted Model 3 analysis revealed a marginally significant difference between the background Ranch Hands and Comparisons in the mean levels of α-1 acid glycoprotein (Table 13-45(e): $p=0.097$). The mean level of α-1 acid glycoprotein, adjusted for percent body fat at the time of duty in SEA and the change in the percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, was lower for the background Ranch Hands than for Comparisons (Table 13-45(e): 55.14 mg/dl vs. 56.38 mg/dl).

Table 13-45.
Analysis of α-1 Acid Glycoprotein (mg/dl)
(Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	*Ranch Hand*	*939*	*56.58*	*0.18 --*	*0.740*
	Comparison	*1,253*	*56.40*		
Officer	Ranch Hand	361	54.08	-0.65 --	0.438
	Comparison	495	54.73		
Enlisted Flyer	Ranch Hand	162	57.81	0.04 --	0.975
	Comparison	196	57.77		
Enlisted Groundcrew	Ranch Hand	416	58.34	0.92 --	0.250
	Comparison	562	57.42		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]	Covariate Remarks[d]
All	*Ranch Hand*	*917*	*55.35*	*0.04 --*	*0.933*	RACE (p=0.016)
	Comparison	*1,232*	*55.30*			OCC (p<0.001)
						DRKYR*ALC (p<0.001)
Officer	Ranch Hand	357	52.38	-0.77 --	0.338	AGE*ALC (p=0.035)
	Comparison	487	53.15			
Enlisted Flyer	Ranch Hand	156	56.26	0.06 --	0.967	
	Comparison	195	56.20			
Enlisted Groundcrew	Ranch Hand	404	57.49	0.82 --	0.316	
	Comparison	550	56.67			

[a] Transformed from natural logarithm scale.

[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

[c] P-values based on difference of means on natural logarithm scale.

[d] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 13-45. (Continued)
Analysis of α-1 Acid Glycoprotein (mg/dl)
(Continuous)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	173	56.19	56.24	0.010	0.0023 (0.0070)	0.745
Medium	170	58.46	58.41			
High	172	57.61	57.61			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[d]			
Initial Dioxin	n	Adj. Mean[ad]	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
Low	170	54.38**	0.098	-0.0134 (0.0081)**	0.097**	INIT*DRKYR (p=0.007) INIT*OCC (p=0.022) RACE (p=0.005) OCC*IC (p=0.020)
Medium	165	55.25**				
High	167	53.30**				

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Slope and standard error based on natural logarithm of α-1 acid glycoprotein versus $\log_2$ (initial dioxin).

[d] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interactions ($p \leq 0.05$); adjusted mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table I-2-32 for further analysis of these interactions.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 13-45. (Continued)
Analysis of α-1 Acid Glycoprotein (mg/dl)
(Continuous)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED					
Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,043	56.38	56.38		
Background RH	369	55.22	55.14	-1.24 --	0.097
Low RH	257	57.13	57.20	0.82 --	0.344
High RH	258	57.69	57.73	1.35 --	0.122
Low plus High RH	515	57.41	57.46	1.08 --	0.108

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED					
Dioxin Category	n	Adj. Mean[ae]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]	Covariate Remarks
Comparison	1,025	54.41**			DXCAT*DRKYR (p=0.017) RACE (p=0.004) OCC (p<0.001) AGE*ALC (p=0.050) ALC*DRKYR (p=0.012) IC*DC (p=0.025)
Background RH	362	53.95**	-0.46 --**	0.535**	
Low RH	251	55.19**	0.78 --**	0.350**	
High RH	251	54.55**	0.15 --**	0.864**	
Low plus High RH	502	54.87**	0.46 --**	0.477**	

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not presented because analysis was performed on natural logarithm scale.

[d] P-value is based on difference of means on natural logarithm scale.

[e] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted mean, difference of adjusted means, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-32 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 13-45. (Continued)
Analysis of α-1 Acid Glycoprotein (mg/dl)
(Continuous)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED						
	Current Dioxin Category Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)		
Model[b]	Low	Medium	High	R^2	Slope (Std. Error)[c]	p-Value
4	55.37 (290)	56.25 (298)	57.83 (296)	0.004	0.0093 (0.0049)	0.060
5	55.42 (294)	55.67 (297)	58.42 (293)	0.007	0.0103 (0.0042)	0.015
6[d]	55.92 (293)	55.73 (297)	57.79 (293)	0.021	0.0055 (0.0045)	0.221

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED							
	Current Dioxin Category Adjusted Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)			
Model[b]	Low	Medium	High	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
4	54.19** (287)	54.12** (290)	53.14** (287)	0.078	-0.0095 (0.0057)**	0.092**	CURR*DRKYR (p=0.042) RACE (p=0.004) ALC (p=0.016) AGE*OCC (p=0.022) OCC*IC (p=0.020)
5	54.19 (290)	53.60 (290)	54.07 (284)	0.072	-0.0040 (0.0048)	0.398	RACE (p=0.005) ALC (p=0.023) DRKYR (p=0.085) AGE*OCC (p=0.021) OCC*IC (p=0.001)
6[e]	54.95 (289)	53.81 (290)	53.44 (284)	0.087	-0.0105 (0.0051)	0.040	RACE (p=0.009) ALC (p=0.043) DRKYR (p=0.093) AGE*OCC (p=0.010) OCC*IC (p=0.001)

[a] Transformed from natural logarithm scale.

[b] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[c] Slope and standard error based on natural logarithm of α-1 acid glycoprotein versus log_2 (current dioxin + 1).

[d] Adjusted for log_2 total lipids.

[e] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-32 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

The interaction between categorized dioxin and lifetime alcohol history was significant in the adjusted Model 3 analysis (Table 13-45(f): $p=0.017$). The final model also contained race, occupation, and three significant covariate-by-covariate interactions: age-by-current alcohol use, current alcohol use-by-lifetime alcohol history, and industrial chemical exposure-by-degreasing chemical exposure. Appendix Table I-2-32 presents adjusted results stratified by lifetime alcohol history. After removing the categorized dioxin-by-lifetime alcohol history interaction from the adjusted analysis, the contrast between the background Ranch Hands and Comparisons became nonsignificant ($p=0.535$). All other contrasts involving the Comparisons remained nonsignificant (Table 13-45(f): $p \geq 0.35$ for all contrasts).

The unadjusted association between current dioxin and α-1 acid glycoprotein was marginally significant in Model 4, significant in Model 5, and not significant in Model 6 (Table 13-45(g): $p=0.060$, Est. Slope=0.0093; $p=0.015$, Est. Slope=0.0103; and $p=0.221$ respectively).

Current dioxin-by-lifetime alcohol history was a significant interaction in the adjusted Model 4 analysis (Table 13-45(h): $p=0.042$). The adjusted Model 4 analysis also contained race, current alcohol use, and two significant covariate-by-covariate interactions: age-by-occupation and occupation-by-industrial chemical exposure. Appendix Table I-2-32 presents adjusted results stratified by lifetime alcohol history for Model 4. For Models 5 and 6, each of the adjusted analyses contained race, current alcohol use, lifetime alcohol history, and two interactions: age-by-occupation and occupation-by-industrial chemical exposure. The association between α-1 acid glycoprotein and current dioxin remained marginally significant in the adjusted Model 4 analysis when the current dioxin-by-lifetime alcohol history interaction was removed from the final model (Table 13-45(h): $p=0.092$, Adj. Slope= -0.0095). However, the direction of the association differed between the unadjusted and adjusted results (increasing in the unadjusted analysis, decreasing in the adjusted analysis). The adjusted Model 5 analysis did not show a significant association between α-1 acid glycoprotein and current dioxin (Table 13-45(h): $p=0.398$), but the adjusted Model 6 analysis found a significant decreasing association (Table 13-45(h): $p=0.040$, Adj. Slope= -0.0105).

Removing occupation from the analyses of Models 4 through 6 changed the statistical significance of adjusted results for these models. With occupation and the current dioxin-by-lifetime alcohol history interaction, the adjusted Model 4 analysis did not reveal a significant association between α-1 acid glycoprotein and current dioxin (Appendix Table I-3-32(c): $p=0.245$). However, the adjusted Model 5 analysis found a marginally significant association between α-1 acid glycoprotein and current dioxin after occupation was removed from the final model (Appendix Table I-3-32(c): $p=0.078$, Adj. Slope=0.0077). When occupation was removed from Model 6, the adjusted analysis did not show α-1 acid glycoprotein to be significantly associated with current dioxin (Appendix Table I-3-32(c): $p=0.572$).

α-1 Acid Glycoprotein (Discrete)

The unadjusted Model 1 analysis did not reveal a significant group difference in the percentage of individuals with high levels of α-1 acid glycoprotein (Table 13-46(a): $p>0.31$

Table 13-46.
Analysis of α-1 Acid Glycoprotein
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	Group	n	Percent High	Est. Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*939*	*2.2*	*0.82 (0.47,1.42)*	*0.570*
	Comparison	*1,253*	*2.7*		
Officer	Ranch Hand	361	1.4	0.52 (0.18,1.47)	0.313
	Comparison	495	2.6		
Enlisted Flyer	Ranch Hand	162	3.7	1.04 (0.34,3.15)	0.999
	Comparison	196	3.6		
Enlisted Groundcrew	Ranch Hand	416	2.4	0.96 (0.42,2.19)	0.999
	Comparison	562	2.5		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	*0.80 (0.46,1.40)***	*0.439***	GROUP*AGE (p=0.018) DRKYR (p=0.014)
Officer	0.51 (0.18,1.43)**	0.199**	
Enlisted Flyer	1.06 (0.35,3.22)**	0.923**	
Enlisted Groundcrew	0.95 (0.41,2.18)**	0.899**	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

** Group-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-33 for further analysis of this interaction.

Table 13-46. (Continued)
Analysis of α-1 Acid Glycoprotein
(Discrete)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	173	2.3	1.17 (0.74,1.85)	0.507
Medium	170	2.4		
High	172	2.3		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
515	1.08 (0.64,1.84)**	0.772**	INIT*OCC (p=0.008) INIT*DC (p=0.029) AGE (p=0.131)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interactions ($p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table I-2-33 for further analysis of these interactions.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 13-46. (Continued)
Analysis of α-1 Acid Glycoprotein
(Discrete)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,043	2.6		
Background RH	369	1.6	0.57 (0.23,1.40)	0.223
Low RH	257	2.3	0.91 (0.37,2.24)	0.837
High RH	258	2.3	0.96 (0.39,2.37)	0.936
Low plus High RH	515	2.3	0.94 (0.47,1.87)	0.852

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,025			DXCAT*AGE ($p<0.001$) DRKYR ($p=0.018$)
Background RH	362	0.53 (0.22,1.33)**	0.177**	
Low RH	251	0.88 (0.36,2.17)**	0.782**	
High RH	251	1.04 (0.42,2.58)**	0.941**	
Low plus High RH	502	0.95 (0.47,1.91)**	0.887**	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interaction ($p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-33 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 13-46. (Continued)
Analysis of α-1 Acid Glycoprotein
(Discrete)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent High/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	1.7 (290)	2.0 (298)	2.4 (296)	1.12 (0.82,1.52)	0.494
5	1.7 (294)	2.0 (297)	2.4 (293)	1.09 (0.83,1.43)	0.555
6[c]	1.7 (293)	2.0 (297)	2.4 (293)	1.12 (0.84,1.51)	0.441

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	864	0.99 (0.69,1.43)**	0.973**	CURR*OCC (p=0.022) DRKYR (p=0.120) OCC*AGE (p=0.001)
5	864	0.99 (0.73,1.34)**	0.960**	CURR*OCC (p=0.025) DRKYR (p=0.125) OCC*AGE (p=0.001)
6[d]	863	1.01 (0.72,1.40)**	0.971**	CURR*OCC (p=0.021) DRKYR (p=0.110) OCC*AGE (p=0.002)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-33 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

for all contrasts). Group-by-age was a significant interaction in the adjusted Model 1 analysis (Table 13-46(b): $p=0.018$). In addition to this interaction, lifetime alcohol history was retained in the final model. Appendix Table I-2-33 presents adjusted results stratified by age. After removing the group-by-lifetime alcohol history interaction from the final model, the adjusted Model 1 analysis did not reveal a significant group contrast (Table 13-46(b): $p>0.19$ for all contrasts).

The unadjusted Model 2 results did not reveal a significant association between α-1 acid glycoprotein and initial dioxin (Table 13-46(c): $p=0.507$). Initial dioxin-by-occupation and initial dioxin-by-degreasing chemical exposure were significant interactions in the adjusted Model 2 analysis (Table 13-46(d): $p=0.008$ and $p=0.029$ respectively). Appendix Table I-2-33 presents adjusted results stratified separately by occupation and degreasing chemical exposure. Age also was retained in the final adjusted model. The adjusted Model 2 analysis did not reveal a significant association between α-1 acid glycoprotein and initial dioxin when the two initial dioxin-by-covariate interactions were removed from the final model (Table 13-46(d): $p=0.772$).

The unadjusted Model 3 analysis did not detect a significant difference between any of the Ranch Hand categories and the Comparison group in the percentage of participants with high α-1 acid glycoprotein levels (Table 13-46(e): $p>0.22$ for all contrasts). The interaction between categorized dioxin and age was significant in the adjusted Model 3 analysis (Table 13-46(f): $p<0.001$). The final model also contained lifetime alcohol history. Appendix Table I-2-33 displays adjusted results stratified by age. Without the categorized dioxin-by-age interaction, the adjusted Model 3 analysis did not show any of the Ranch Hand categories to differ significantly from the Comparisons (Table 13-46(f): $p>0.17$ for all contrasts).

The unadjusted analyses for Models 4 through 6 did not detect a significant association between α-1 acid glycoprotein and current dioxin (Table 13-46(g): $p>0.44$ for all analyses). Each of the adjusted analyses for Models 4 through 6 contained a significant interaction between current dioxin and occupation (Table 13-46(h): $p=0.022$, $p=0.025$, and $p=0.021$ for Models 4, 5, and 6 respectively). In addition to this interaction, each of the final models contained lifetime alcohol history and the interaction between occupation and age. Appendix Table I-2-33 displays adjusted results stratified by occupation for Models 4 through 6. The adjusted analyses for Models 4, 5, and 6 did not show a significant association between α-1 acid glycoprotein and current dioxin when the current dioxin-by-occupation interaction was removed from each of the analyses (Table 13-46(h): $p>0.96$ for all analyses).

α-1 Antitrypsin (Continuous)

The unadjusted Model 1 analysis detected a marginally significant overall group difference in the mean levels of α-1 antitrypsin (Table 13-47(a): $p=0.077$). The mean level of α-1 antitrypsin was higher for the Ranch Hands than for the Comparisons (151.59 mg/dl vs. 149.48 mg/dl). The stratified occupation analysis did not reveal a significant group contrast (Table 13-47(a): $p>0.18$ for any of the stratified contrasts).

Table 13-47.
Analysis of α-1 Antitrypsin (mg/dl)
(Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Mean	Difference of Means (95% C.I.)	p-Value
All	*Ranch Hand*	*939*	*151.59*	*2.12 (-0.23,4.46)*	*0.077*
	Comparison	*1,253*	*149.48*		
Officer	Ranch Hand	361	146.98	1.08 (-2.60,4.77)	0.564
	Comparison	495	145.89		
Enlisted Flyer	Ranch Hand	162	156.91	3.19 (-2.76,9.13)	0.294
	Comparison	196	153.72		
Enlisted Groundcrew	Ranch Hand	416	153.53	2.38 (-1.10,5.86)	0.181
	Comparison	562	151.15		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Group	n	Adj. Mean	Difference of Adj. Means (95% C.I.)	p-Value	Covariate Remarks[a]
All	*Ranch Hand*	*917*	*148.79*	*2.16 (-0.12,4.44)*	*0.063*	AGE ($p<0.001$)
	Comparison	*1,232*	*146.63*			RACE ($p=0.011$)
Officer	Ranch Hand	357	142.60	1.40 (-2.26,5.05)	0.454	OCC ($p<0.001$)
	Comparison	487	141.20			DRKYR ($p<0.001$)
Enlisted Flyer	Ranch Hand	156	152.05	3.49 (-2.13,9.12)	0.223	WINE ($p<0.001$)
	Comparison	195	148.56			DC ($p=0.037$)
Enlisted Groundcrew	Ranch Hand	404	152.18	2.34 (-1.08,5.77)	0.180	
	Comparison	550	149.83			

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 13-47. (Continued)
Analysis of α-1 Antitrypsin (mg/dl)
(Continuous)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[a]		
Initial Dioxin	n	Mean	Adj. Mean[a]	R^2	Slope (Std. Error)	p-Value
Low	173	148.46	148.13	0.020	0.9889 (0.8901)	0.267
Medium	170	153.74	153.80			
High	172	151.65	151.93			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[b]			
Initial Dioxin	n	Adj. Mean[b]	R^2	Adj. Slope (Std. Error)	p-Value	Covariate Remarks
Low	170	142.66**	0.116	0.1019 (1.0141)**	0.920**	INIT*IC (p=0.016) INIT*DC (p=0.027)
Medium	165	145.54**				AGE (p=0.007) RACE (p=0.016) DRKYR (p=0.008)
High	167	143.42**				OCC*WINE (p=0.008) IC*WINE (p=0.016)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interactions ($0.01 < p \leq 0.05$); adjusted mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table I-2-34 for further analysis of these interactions.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 13-47. (Continued)
Analysis of α-1 Antitrypsin (mg/dl)
(Continuous)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED					
Dioxin Category	n	Mean	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)	p-Value
Comparison	1,043	149.64	149.67		
Background RH	369	151.60	151.35	1.68 (-1.60,4.96)	0.315
Low RH	257	151.44	151.17	1.50 (-2.25,5.25)	0.433
High RH	258	151.10	151.60	1.93 (-1.82,5.67)	0.314
Low plus High RH	515	151.27	151.39	1.71 (-1.19,4.62)	0.248

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED					
Dioxin Category	n	Adj. Mean[b]	Difference of Adj. Mean vs. Comparisons (95% C.I.)	p-Value	Covariate Remarks
Comparison	1,025	146.42			AGE ($p<0.001$) RACE ($p=0.013$) OCC ($p<0.001$) DRKYR ($p<0.001$) WINE ($p<0.001$) DC ($p=0.016$)
Background RH	362	150.72	4.30 (1.03,7.56)	0.010	
Low RH	251	147.32	0.90 (-2.77,4.56)	0.632	
High RH	251	146.25	-0.17 (-3.96,3.62)	0.929	
Low plus High RH	502	146.78	0.36 (-2.50,3.23)	0.804	

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 13-47. (Continued)
Analysis of α-1 Antitrypsin (mg/dl)
(Continuous)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED						
	Current Dioxin Category Mean/(n)			Analysis Results for Log_2 (Current Dioxin + 1)		
Model[a]	Low	Medium	High	R^2	Slope (Std. Error)	p-Value
4	152.72 (290)	150.29 (298)	151.25 (296)	<0.001	-0.3957 (0.6371)	0.535
5	153.39 (294)	148.52 (297)	152.35 (293)	0.001	-0.6233 (0.5469)	0.255
6[b]	152.79 (293)	148.49 (297)	152.70 (293)	0.001	-0.2962 (0.5870)	0.614

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED							
	Current Dioxin Category Adjusted Mean/(n)			Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	Low	Medium	High	R^2	Adj. Slope (Std. Error)	p-Value	Covariate Remarks
4	150.45** (287)	145.06** (290)	142.35** (287)	0.097	-2.0421 (0.7054)**	0.004**	CURR*OCC (p=0.034) CURR*DC (p=0.013) AGE (p<0.001) RACE (p=0.015) DRKYR (p=0.004) OCC*WINE (p=0.027) IC*WINE (p=0.033)
5	150.87** (290)	143.59** (290)	144.05** (284)	0.102	-2.1148 (0.5949)**	<0.001**	CURR*OCC (p=0.032) CURR*DC (p=0.007) AGE (p<0.001) RACE (p=0.013) DRKYR (p=0.003) OCC*WINE (p=0.030) IC*WINE (p=0.028)
6[c]	150.01** (289)	143.42** (290)	144.52** (284)	0.099	-1.7231 (0.6417)**	0.007**	CURR*OCC (p=0.028) CURR*DC (p=0.012) AGE (p<0.001) RACE (p=0.013) DRKYR (p=0.003) OCC*WINE (p=0.036) IC*WINE (p=0.026)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Adjusted for log_2 total lipids.

[c] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interactions ($p \leq 0.05$); adjusted mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table I-2-34 for further analysis of these interactions.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

The adjusted Model 1 results were similar to the unadjusted results. The adjusted analysis revealed a marginally significant overall group contrast (Table 13-47: p=0.063) but did not show any significant contrasts within any of the occupation strata (Table 13-47(b): p>0.18 for all stratified group contrasts). The final model contained age, race, occupation, lifetime alcohol history, current wine use, and degreasing chemical exposure.

The unadjusted Model 2 results did not reveal a significant association between α-1 antitrypsin and initial dioxin (Table 13-47(c): p=0.267). Initial dioxin-by-industrial chemical exposure and initial dioxin-by-degreasing chemical exposure were significant interactions in the adjusted Model 2 analysis (Table 13-47(d): p=0.016 and p=0.027 respectively). Appendix Table I-2-34 presents adjusted results stratified separately by industrial chemical exposure and degreasing chemical exposure. The final model also contained age, race, lifetime alcohol history, and two significant covariate-by-covariate interactions: occupation-by-current wine use and industrial chemical exposure-by-current wine use. The adjusted Model 2 analysis did not show a significant association between α-1 antitrypsin and current dioxin when the two initial dioxin-by-current dioxin interactions were removed from the final model (Table 13-47(d): p=0.920).

The unadjusted Model 3 analysis did not show a significant difference between any of the Ranch Hand categories and the Comparison group in the mean levels of α-1 antitrypsin (Table 13-47(e): p>0.24 for all contrasts). After adjusting for age, race, occupation, lifetime alcohol history, current wine use, and degreasing chemical exposure, the mean for the background Ranch Hands became significantly larger than the mean for the Comparison group (Table 13-47(f): 150.72 mg/dl vs. 146.42 mg/dl, p=0.010). All other contrasts with the Comparisons remained nonsignificant.

When occupation was removed from the Model 3 analysis, the adjusted results corresponded to the unadjusted results. The adjusted Model 3 analysis without occupation did not show the Comparisons to be significantly different from any of the Ranch Hand categories (Appendix Table I-3-34(b): p>0.10 for all contrasts).

The unadjusted analyses for Models 4 through 6 did not reveal a significant association between α-1 antitrypsin and current dioxin (Table 13-47(g): p>0.25 for all analyses). Current dioxin-by-occupation and current dioxin-by-degreasing chemical exposure were significant covariates in each of the adjusted analyses of Models 4 through 6 (Table 13-47(h): p=0.034, p=0.013; p=0.032, p=0.007; and p=0.028, p=0.012 for Models 4, 5, and 6 respectively). Appendix Table I-2-34 presents adjusted results stratified separately by occupation and degreasing chemical exposure for Models 4 through 6. In addition to the two current dioxin-by-covariate interactions, each of the adjusted analyses for Models 4 through 6 also contained age, race, lifetime alcohol history, and two significant covariate-by-covariate interactions: occupation-by-current wine use and industrial chemical exposure-by-current wine use.

After removing the two current dioxin-by-covariate interactions from the final models, each of the adjusted analyses for Models 4 through 6 uncovered a significant inverse association between α-1 antitrypsin and current dioxin (Table 13-47(h): p=0.004, Adj.

Slope=-2.0421; p<0.001, Adj. Slope=-2.1148; and p=0.007, Adj. Slope=-1.7231 for Models 4, 5, and 6 respectively).

In the followup models excluding occupation, the adjusted results for Models 4 and 6 became nonsignificant (Appendix Table I-3-34(c): p>0.25 for both analyses), while the adjusted result for Model 5 became marginally significant (Appendix Table I-3-34(c): p=0.060, Adj. Slope=-1.0583).

α-1 Antitrypsin (Discrete)

The unadjusted and adjusted Model 1 analyses did not reveal a significant group difference in either the percentage of participants with low α-1 antitrypsin levels or the percentage of participants with high α-1 antitrypsin levels (Table 13-48(a,b): p>0.22 for all contrasts). The final adjusted model contained age, race, occupation, and current wine use.

Examination of the unadjusted Model 2 results did not reveal a significant association between the percentage of individuals with low α-1 antitrypsin levels and initial dioxin or between the percentage of individuals with high α-1 antitrypsin levels and current dioxin (Table 13-48(c): p>0.40 for both associations). The unadjusted and adjusted results were identical because no covariates were retained in the final model.

The unadjusted and adjusted Model 3 analyses did not reveal a significant difference between any of the Ranch Hand categories and the Comparison group in the percentage of individuals with low α-1 antitrypsin levels or in the percentage of participants with α-1 high antitrypsin levels (Table 13-48(e): p>0.13 for all contrasts). The adjusted analysis for Model 3 contained age, race, and occupation.

The unadjusted analyses of Models 4 through 6 did not reveal a significant association between the percentage of individuals with low α-1 antitrypsin levels and current dioxin (Table 13-48(g): p>0.23 for Models 4 through 6). However, the unadjusted analyses for Models 4 and 5 detected a marginally significant association between the percentage of participants with high α-1 antitrypsin levels and current dioxin (Table 13-48(g): p=0.082, Est. RR=0.70, 95% C.I.=[0.47, 1.05] and p=0.056, Est. RR=0.76, 95% C.I.=[0.57, 1.01]). The unadjusted Model 6 analysis did not reveal a significant association between the percentage of participants with high α-1 antitrypsin levels and current dioxin (Table 13-48(g): p=0.390).

The adjusted analyses of Models 4 through 6 generally supported the findings of the unadjusted analyses. After adjusting for degreasing chemicals in Models 4 and 5, the association between current dioxin and low α-1 antitrypsin levels remained nonsignificant, while the association with high α-1 antitrypsin remained marginally significant in Model 4 (Table 13-48(h): p=0.054, Adj. RR=0.67, 95% C.I.=[0.45, 1.01]) but became significant in Model 5 (p=0.035, Adj. RR=0.74, 95% C.I.=[0.55, 0.98]). The adjusted analysis for Model 6 paralleled the unadjusted analysis because no covariates were retained in the final model.

Table 13-48.
Analysis of α-1 Antitrypsin
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED									
			Percent			Low vs. Normal		High vs. Normal	
Occupational Category	Group	n	Low	Normal	High	Est. Relative Risk (95% C.I.)	p-Value	Est. Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*939*	*2.2*	*96.0*	*1.8*	*1.35 (0.73,2.49)*	*0.419*	*1.43 (0.72,2.85)*	*0.393*
	Comparison	*1,253*	*1.7*	*97.1*	*1.3*				
Officer	Ranch Hand	361	3.6	94.5	1.9	1.40 (0.64,3.06)	0.520	1.96 (0.62,6.22)	0.387
	Comparison	495	2.6	96.4	1.0				
Enlisted Flyer	Ranch Hand	162	1.2	96.9	1.9	2.45 (0.22,27.22)	0.866	1.22 (0.24,6.14)	0.999
	Comparison	196	0.5	98.0	1.5				
Enlisted Groundcrew	Ranch Hand	416	1.4	96.9	1.7	1.16 (0.39,3.49)	0.999	1.19 (0.43,3.30)	0.947
	Comparison	562	1.3	97.3	1.4				

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED					
	Low vs. Normal		High vs. Normal		
Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	*1.34 (0.73,2.49)*	*0.347*	*1.35 (0.66,2.73)*	*0.409*	AGE (p<0.001) RACE (p=0.031) OCC (p=0.048) WINE (p=0.039)
Officer	1.37 (0.62,3.00)	0.434	2.06 (0.64,6.61)	0.224	
Enlisted Flyer	2.50 (0.23,27.60)	0.456	1.19 (0.24,6.05)	0.831	
Enlisted Groundcrew	1.13 (0.38,3.41)	0.824	0.98 (0.33,2.90)	0.975	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 13-48. (Continued)
Analysis of α-1 Antitrypsin
(Discrete)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED									
Initial Dioxin Category Summary Statistics					Analysis Results for Log_2 (Initial Dioxin)[a]				
		Percent			Low vs. Normal		High vs. Normal		
Initial Dioxin Category	n	Low	Normal	High	Est. Relative Risk (95% C.I.)[b]	p-Value	Est. Relative Risk (95% C.I.)[b]	p-Value	
Low	173	1.7	96.5	1.7	0.90 (0.51,1.57)	0.703	0.75 (0.38,1.47)	0.404	
Medium	170	1.2	97.7	1.2					
High	172	1.7	97.7	0.6					

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED					
	Analysis Results for Log_2 (Initial Dioxin)[a]				
	Low vs. Normal		High vs. Normal		
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
515	0.90 (0.51,1.57)	0.703	0.75 (0.38,1.47)	0.404	

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 13-48. (Continued)
Analysis of α-1 Antitrypsin
(Discrete)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED								
		Percent			Low vs. Normal		High vs. Normal	
Dioxin Category	n	Low	Normal	High	Est. Relative Risk (95% C.I.)[ab]	p-Value	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,043	1.9	96.7	1.3				
Background RH	369	3.0	94.9	2.2	1.51 (0.71,3.22)	0.283	1.72 (0.70,4.22)	0.234
Low RH	257	1.6	96.5	2.0	0.83 (0.28,2.45)	0.736	1.24 (0.43,3.53)	0.692
High RH	258	1.6	98.1	0.4	0.83 (0.28,2.45)	0.735	0.20 (0.02,1.67)	0.138
Low plus High RH	515	1.6	97.3	1.2	0.83 (0.36,1.90)	0.658	0.71 (0.26,1.92)	0.498

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED						
		Low vs. Normal		High vs. Normal		
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,043					AGE (p=0.007) RACE (p=0.056) OCC (p=0.040)
Background RH	369	1.24 (0.57,2.66)	0.586	1.81 (0.71,4.57)	0.211	
Low RH	257	0.92 (0.31,2.75)	0.881	1.16 (0.40,3.38)	0.791	
High RH	258	1.19 (0.37,3.81)	0.765	0.23 (0.03,1.80)	0.160	
Low plus High RH	515	1.03 (0.44,2.42)	0.945	0.70 (0.26,1.93)	0.493	

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of duty in SEA and change in body fat from the time of duty in SEA to the date of the blood draw for dioxin.
[c] Adjusted for percent body fat at the time of duty in SEA, change in body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 13-48. (Continued)
Analysis of α-1 Antitrypsin
(Discrete)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED									
	Current Dioxin Category Summary Statistics					Analysis Results for Log_2 (Current Dioxin + 1)			
			Percent			Low vs. Normal		High vs. Normal	
Model[a]	Current Dioxin Category	n	Low	Normal	High	Est. Relative Risk (95% C.I.)[b]	p-Value	Est. Relative Risk (95% C.I.)[b]	p-Value
4	Low	290	3.1	94.1	2.8	0.82 (0.59,1.14)	0.236	0.70 (0.47,1.05)	0.082
	Medium	298	1.7	97.0	1.3				
	High	296	1.7	97.6	0.7				
5	Low	294	3.1	94.2	2.7	0.88 (0.67,1.14)	0.335	0.76 (0.57,1.01)	0.056
	Medium	297	1.4	97.3	1.4				
	High	293	2.1	97.3	0.7				
6[c]	Low	293	3.1	94.5	2.4	0.88 (0.67,1.15)	0.344	0.86 (0.62,1.20)	0.390
	Medium	297	1.4	97.3	1.4				
	High	293	2.1	97.3	0.7				

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for $\log_2$ total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for $\log_2$ total lipids.

Note: Model 4: Low = $\leq$ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = $\leq$ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 13-48. (Continued)
Analysis of α-1 Antitrypsin
(Discrete)

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED						
		Analysis Results for Log_2 (Current Dioxin)				
		Low vs. Normal		High vs. Normal		
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	884	0.88 (0.62,1.24)	0.449	0.67 (0.45,1.01)	0.054	DC (p=0.147)
5	884	0.93 (0.70,1.23)	0.604	0.74 (0.55,0.98)	0.035	DC (p=0.134)
6[c]	883	0.88 (0.67,1.15)	0.344	0.86 (0.62,1.20)	0.390	

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

α-2 Macroglobulin (Continuous)

The unadjusted and adjusted Model 1 analyses did not reveal a significant group difference in the mean levels of α-2 macroglobulin (Table 13-49(a,b): $p>0.21$ for all contrasts). The final model contained age, race, occupation, lifetime alcohol history, and current alcohol use.

Examination of the unadjusted Model 2 results did not show a significant association between α-2 macroglobulin and initial dioxin (Table 13-49(c): $p=0.784$). The adjusted Model 2 analysis contained a significant interaction between initial dioxin and age (Table 13-49(d): $p=0.033$). Race, lifetime alcohol history, and current alcohol use also were significant covariates in the final model. Appendix Table I-2-35 presents adjusted results stratified by age. When the initial dioxin-by-age interaction was removed from the final model, the adjusted Model 2 analysis did not reveal a significant association between α-2 macroglobulin and initial dioxin (Table 13-49(d): $p=0.165$).

The unadjusted Model 3 results did not reveal a significant difference between any of the Ranch Hand categories and the Comparison group in the mean levels of α-2 macroglobulin (Table 13-49(e): $p>0.17$ for all analyses).

After covariate adjustment, the mean α-2 macroglobulin became marginally lower in the low plus high Ranch Hand category relative to the Comparison group (Table 13-49(f): $p=0.078$, 127.32 mg/dl vs. 129.92 mg/dl). All other contrasts involving Comparisons remained nonsignificant. The final model contained age, race, occupation, lifetime alcohol history, and current alcohol use.

Without occupation in the final model, the adjusted results for Model 3 changed slightly. After removing occupation, the adjusted Model 3 analysis did not show any of the Ranch Hand categories to be significantly different from the Comparison group (Appendix Table I-3-36(a): $p>0.12$ for all contrasts).

Each of the unadjusted analyses for Models 4 through 6 uncovered a significant inverse association between α-2 macroglobulin and current dioxin (Table 13-49(g): $p=0.029$, Est. Slope=-0.0111; $p=0.046$, Est. Slope=-0.0087; and $p=0.018$, Est. Slope=-0.0111 for Models 4, 5, and 6 respectively).

After covariate adjustment, the adjusted results supported the unadjusted findings. Each of the adjusted analyses detected a significant inverse association between α-2 macroglobulin and current dioxin (Table 13-49(h): $p=0.006$, Adj. Slope=-0.0155; $p=0.008$, Adj. Slope= -0.0126; and $p=0.007$, Adj. Slope=-0.0139 for Models 4, 5, and 6 respectively). All of the adjusted analyses for Models 4 through 6 contained age, race, occupation, lifetime alcohol history, and current alcohol use.

Removing occupation from the analyses of Models 4 through 6 produced markedly different adjusted results for these three models. Without occupation, the association between macroglobulin and current dioxin became nonsignificant for each model (Appendix Table I-3-36(b): $p>0.47$ for each analysis).

Table 13-49.
Analysis of α-2 Macroglobulin (mg/dl)
(Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	*Ranch Hand*	*939*	*133.35*	*-0.65 --*	*0.607*
	Comparison	*1,253*	*134.00*		
Officer	Ranch Hand	361	132.08	-1.02 --	0.609
	Comparison	495	133.10		
Enlisted Flyer	Ranch Hand	162	135.74	-3.32 --	0.276
	Comparison	196	139.06		
Enlisted Groundcrew	Ranch Hand	416	133.53	0.47 --	0.803
	Comparison	562	133.06		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]	Covariate Remarks[d]
All	*Ranch Hand*	*917*	*128.91*	*-0.84 --*	*0.476*	AGE ($p<0.001$)
	Comparison	*1,232*	*129.75*			RACE ($p<0.001$)
						OCC ($p<0.001$)
Officer	Ranch Hand	357	123.85	-1.17 --	0.518	DRKYR ($p=0.054$)
	Comparison	487	125.02			ALC ($p=0.020$)
Enlisted Flyer	Ranch Hand	156	129.05	-3.63 --	0.216	
	Comparison	195	132.68			
Enlisted Groundcrew	Ranch Hand	404	133.00	0.53 --	0.770	
	Comparison	550	132.47			

[a] Transformed from natural logarithm scale.

[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

[c] P-values based on difference of means on natural logarithm scale.

[d] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 13-49. (Continued)
Analysis of α-2 Macroglobulin (mg/dl)
(Continuous)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	173	131.43	130.79	0.051	-0.0020 (0.0073)	0.784
Medium	170	133.23	133.30			
High	172	131.43	132.01			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[d]			
Initial Dioxin	n	Adj. Mean[ad]	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
Low	170	122.50**	0.150	0.0105 (0.0075)**	0.165**	INIT*AGE (p=0.033) RACE (p=0.003) DRKYR (p=0.031) ALC (p=0.018)
Medium	165	126.72**				
High	167	129.34**				

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Slope and standard error based on natural logarithm of α-2 macroglobulin versus $\log_2$ (initial dioxin).

[d] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-35 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 13-49. (Continued)
Analysis of α-2 Macroglobulin (mg/dl)
(Continuous)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED					
Dioxin Category	**n**	**Mean[a]**	**Adj. Mean[ab]**	**Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]**	**p-Value[d]**
Comparison	1,043	134.23	134.27		
Background RH	369	134.46	134.15	-0.12 --	0.944
Low RH	257	132.86	132.47	-1.80 --	0.368
High RH	258	131.19	131.85	-2.42 --	0.226
Low plus High RH	515	132.02	132.16	-2.11 --	0.173

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED					
Dioxin Category	**n**	**Adj. Mean[ae]**	**Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]**	**p-Value[d]**	**Covariate Remarks**
Comparison	1,025	129.92			AGE ($p<0.001$) RACE ($p<0.001$) OCC ($p<0.001$) DRKYR ($p=0.078$) ALC ($p=0.003$)
Background RH	362	130.31	0.39 --	0.819	
Low RH	251	126.98	-2.95 --	0.118	
High RH	251	127.67	-2.25 --	0.249	
Low plus High RH	502	127.32	-2.60 --	0.078	

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not presented because analysis was performed on natural logarithm scale.

[d] P-value is based on difference of means on natural logarithm scale.

[e] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin $\leq$ 10 ppt.
Background (Ranch Hand): Current Dioxin $\leq$ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin $\leq$ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 13-49. (Continued)
Analysis of α-2 Macroglobulin (mg/dl)
(Continuous)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED						
	Current Dioxin Category Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)		
Model[b]	Low	Medium	High	R^2	Slope (Std. Error)[c]	p-Value
4	134.97 (290)	133.02 (298)	131.18 (296)	0.005	-0.0111 (0.0051)	0.029
5	135.18 (294)	131.91 (297)	132.04 (293)	0.005	-0.0087 (0.0043)	0.046
6[d]	135.74 (293)	131.99 (297)	131.22 (293)	0.008	-0.0111 (0.0047)	0.018

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED							
	Current Dioxin Category Adjusted Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)			
Model[b]	Low	Medium	High	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
4	131.92 (287)	127.16 (290)	125.82 (287)	0.115	-0.0155 (0.0056)	0.006	AGE ($p<0.001$) RACE ($p=0.006$) OCC ($p<0.001$) DRKYR ($p=0.016$) ALC ($p=0.039$)
5	132.13 (290)	126.31 (290)	126.83 (284)	0.114	-0.0126 (0.0047)	0.008	AGE ($p<0.001$) RACE ($p=0.006$) OCC ($p<0.001$) DRKYR ($p=0.017$) ALC ($p=0.043$)
6[e]	132.51 (289)	126.48 (290)	126.43 (284)	0.114	-0.0139 (0.0051)	0.007	AGE ($p<0.001$) RACE ($p=0.008$) OCC ($p<0.001$) DRKYR ($p=0.017$) ALC ($p=0.033$)

[a] Transformed from natural logarithm scale.

[b] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[c] Slope and standard error based on natural logarithm of α-2 macroglobulin versus log_2 (current dioxin + 1).

[d] Adjusted for log_2 total lipids.

[e] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = $\leq$ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = $\leq$ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

α-2 Macroglobulin (Discrete)

The unadjusted and adjusted Model 1 analyses did not reveal a significant group difference in the percentage of participants with high α-2 macroglobulin levels (Table 13-50(a,b): $p>0.42$ for all contrasts). Age, occupation, and degreasing chemical exposure were significant covariates in the adjusted Model 1 analysis.

The unadjusted Model 2 results did not reveal a significant association between α-2 macroglobulin and current dioxin (Table 13-50(c): $p=0.508$). The unadjusted and adjusted results were identical because no covariates were retained in the final model.

The unadjusted and adjusted Model 3 analyses did not show a significant group difference between any of the Ranch Hand categories and the Comparison group in the percentage of individuals with high α-2 macroglobulin levels (Table 13-50(e,f): $p>0.46$ for all contrasts). The adjusted Model 3 analysis retained age, occupation, degreasing chemical exposure, and current alcohol use in the final model.

The unadjusted and adjusted analyses for Models 4 through 6 did not reveal a significant association between α-2 macroglobulin and current dioxin (Table 13-50(g,h): $p>0.62$ for all analyses). No covariates were retained in any of the adjusted analyses for Models 4 through 6.

Apolipoprotein B (Continuous)

The unadjusted and adjusted Model 1 analyses did not reveal a significant group difference in the mean levels of apolipoprotein B (Table 13-51(a,b): $p\geq0.12$ for all contrasts). The adjusted Model 1 analysis contained current alcohol use and two interactions: age-by-lifetime alcohol history and race-by-occupation.

Examination of the unadjusted Model 2 results did not show a significant association between apolipoprotein B and initial dioxin (Table 13-51(c): $p=0.112$). Initial dioxin-by-age was a significant interaction in the adjusted analysis of Model 2 (Table 13-51(d): $p=0.038$). Appendix Table I-2-36 presents adjusted results stratified by age. In contrast to the unadjusted analysis, the adjusted Model 2 analysis detected a significant positive association between apolipoprotein B and initial dioxin when the initial dioxin-by-age interaction was removed from the final model (Table 13-51(d): $p=0.018$, Adj. Slope=0.0202).

The unadjusted and adjusted Model 3 analyses did not reveal a significant difference between any of the Ranch Hand categories and the Comparison group in the mean levels of apolipoprotein B (Table 13-51(e,f): $p>0.11$ for all contrasts). The adjusted Model 3 analysis contained current alcohol use, degreasing chemical exposure, and two interactions: race-by-occupation and age-by-lifetime alcohol history.

The unadjusted analyses for Models 4 and 5 revealed a significant positive association between apolipoprotein B and current dioxin (Table 13-51(g): $p=0.016$, Est. Slope=0.0138 and $p<0.001$, Est. Slope=0.0244 for Models 4 and 5 respectively). The unadjusted Model

Table 13-50.
Analysis of α-2 Macroglobulin
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent High**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	*Ranch Hand*	*939*	*0.4*	*0.89 (0.25,3.16)*	*0.999*
	Comparison	*1,253*	*0.5*		
Officer	Ranch Hand	361	0.0	--	--
	Comparison	495	0.4		
Enlisted Flyer	Ranch Hand	162	0.6	0.60 (0.05,6.71)	0.999
	Comparison	196	1.0		
Enlisted Groundcrew	Ranch Hand	416	0.7	2.03 (0.34,12.23)	0.735
	Comparison	562	0.4		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	*0.96 (0.26,3.55)*	*0.952*	AGE ($p<0.001$) OCC ($p=0.011$) DC ($p=0.013$)
Officer	--	--	
Enlisted Flyer	0.86 (0.07,10.63)	0.906	
Enlisted Groundcrew	2.18 (0.32,14.70)	0.424	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

--: Adjusted relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities.

Table 13-50. (Continued)
Analysis of α-2 Macroglobulin
(Discrete)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	173	0.0	1.38 (0.53,3.59)	0.508
Medium	170	0.6		
High	172	0.6		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
515	1.38 (0.53,3.59)	0.508	

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 13-50. (Continued)
Analysis of α-2 Macroglobulin
(Discrete)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,043	0.6		
Background RH	369	0.3	0.51 (0.06,4.36)	0.542
Low RH	257	0.0	--	--
High RH	258	0.8	1.11 (0.21,5.88)	0.905
Low plus High RH	515	0.4	0.55 (0.11,2.86)	0.479

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,027			AGE (p=0.006) OCC (p=0.133) DC (p=0.022) ALC (p=0.108)
Background RH	367	0.50 (0.05,4.72)	0.546	
Low RH	254	--	--	
High RH	254	1.13 (0.20,6.35)	0.890	
Low plus High RH	508	0.53 (0.10,2.85)	0.462	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

--: Adjusted relative risk, confidence interval, and p-value not presented due to the sparse number of abnormalities.

Note: RH = Ranch Hand.
Comparison: Current Dioxin $\leq$ 10 ppt.
Background (Ranch Hand): Current Dioxin $\leq$ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin $\leq$ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 13-50. (Continued)
Analysis of α-2 Macroglobulin
(Discrete)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent High/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	0.3 (290)	0.0 (298)	0.7 (296)	1.18 (0.56,2.46)	0.668
5	0.3 (294)	0.0 (297)	0.7 (293)	1.18 (0.61,2.28)	0.623
6[c]	0.3 (293)	0.0 (297)	0.7 (293)	1.11 (0.55,2.27)	0.771

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	884	1.18 (0.56,2.46)	0.668	
5	884	1.18 (0.61,2.28)	0.623	
6[c]	883	1.11 (0.55,2.27)	0.771	

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 13-51.
Analysis of Apolipoprotein B (mg/dl)
(Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Mean[a]**	**Difference of Means (95% C.I.)[b]**	**p-Value[c]**
All	*Ranch Hand*	*939*	*147.55*	*-0.22 --*	*0.888*
	Comparison	*1,253*	*147.77*		
Officer	Ranch Hand	361	144.35	-0.02 --	0.993
	Comparison	495	144.37		
Enlisted Flyer	Ranch Hand	162	151.04	-5.50 --	0.137
	Comparison	196	156.55		
Enlisted Groundcrew	Ranch Hand	416	149.02	1.20 --	0.621
	Comparison	562	147.82		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED						
Occupational Category	**Group**	**n**	**Adj. Mean[a]**	**Difference of Adj. Means (95% C.I.)[b]**	**p-Value[c]**	**Covariate Remarks[d]**
All	*Ranch Hand*	*917*	*151.01*	*-0.65 --*	*0.685*	ALC (p=0.143)
	Comparison	*1,232*	*151.66*			AGE*DRKYR (p=0.044)
Officer	Ranch Hand	357	154.09	-0.22 --	0.934	RACE*OCC (p=0.027)
	Comparison	487	154.31			
Enlisted Flyer	Ranch Hand	156	149.06	-6.17 --	0.120	
	Comparison	195	155.23			
Enlisted Groundcrew	Ranch Hand	404	147.92	0.97 --	0.678	
	Comparison	550	146.95			

[a] Transformed from natural logarithm scale.

[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

[c] P-values based on difference of means on natural logarithm scale.

[d] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 13-51. (Continued)
Analysis of Apolipoprotein B (mg/dl)
(Continuous)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	173	147.71	147.70	0.005	0.0130 (0.0082)	0.112
Medium	170	147.44	147.44			
High	172	151.73	151.75			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[d]			
Initial Dioxin	n	Adj. Mean[ad]	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
Low	173	146.25**	0.028	0.0202 (0.0085)**	0.018**	INIT*AGE (p=0.038)
Medium	170	147.10**				
High	172	153.62**				

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Slope and standard error based on natural logarithm of apolipoprotein B versus $\log_2$ (initial dioxin).

[d] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-36 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 13-51. (Continued)
Analysis of Apolipoprotein B (mg/dl)
(Continuous)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED					
Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,043	147.58	147.56		
Background RH	369	144.89	145.06	-2.50 --	0.246
Low RH	257	146.14	146.21	-1.35 --	0.585
High RH	258	151.81	151.54	3.97 --	0.115
Low plus High RH	515	148.95	148.85	1.29 --	0.505

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED					
Dioxin Category	n	Adj. Mean[ae]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]	Covariate Remarks
Comparison	1,025	152.03			ALC (p=0.041) DC (p=0.117) RACE*OCC (p=0.023) AGE*DRKYR (p=0.049)
Background RH	362	150.68	-1.34 --	0.556	
Low RH	251	149.75	-2.27 --	0.373	
High RH	251	154.41	2.38 --	0.374	
Low plus High RH	502	152.06	0.04 --	0.986	

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not presented because analysis was performed on natural logarithm scale.

[d] P-value is based on difference of means on natural logarithm scale.

[e] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 13-51. (Continued)
Analysis of Apolipoprotein B (mg/dl)
(Continuous)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED						
	Current Dioxin Category Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)		
Model[b]	Low	Medium	High	R^2	Slope (Std. Error)[c]	p-Value
4	144.54 (290)	146.30 (298)	150.92 (296)	0.007	0.0138 (0.0057)	0.016
5	140.51 (294)	148.04 (297)	153.47 (293)	0.028	0.0244 (0.0048)	<0.001
6[d]	148.04 (293)	148.80 (297)	144.84 (293)	0.271	-0.0022 (0.0045)	0.624

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED							
	Current Dioxin Category Adjusted Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)			
Model[b]	Low	Medium	High	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
4	144.27 (290)	144.81 (298)	149.92 (296)	0.019	0.0132 (0.0059)	0.026	AGE (p=0.018) DC (p=0.011)
5	140.13** (294)	146.83** (297)	152.78** (293)	0.046	0.0246 (0.0050)**	<0.001**	CURR*AGE (p=0.017) DC (p=0.059)
6[e]	147.53 (289)	148.09 (290)	143.76 (284)	0.280	-0.0026 (0.0048)	0.581	AGE (p=0.117) DRKYR (p=0.077) DC (p=0.059)

[a] Transformed from natural logarithm scale.

[b] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[c] Slope and standard error based on natural logarithm of apoliprotein B versus log_2 (current dioxin + 1).

[d] Adjusted for log_2 total lipids.

[e] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-36 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

6 analysis did not show a significant association (Table 13-51(g): p=0.624). The nonsignificant association in Model 6 resulted from the high correlation between log lipids and apolipoprotein B, which can be inferred from the difference between the R-squares in Models 5 and 6. The R-square jumped from 0.028 in Model 5 to 0.271 in Model 6, the only difference in the two models being the inclusion of log lipids as a forced adjusting covariate in Model 6.

The adjusted results for Models 4 through 6 paralleled the unadjusted results. After adjusting for age and degreasing chemical exposure, the Model 4 analysis found a significant positive association between apolipoprotein B and current dioxin (Table 13-51(h): p=0.026, Adj. Slope=0.0132). Current dioxin by age was a significant interaction in the adjusted Model 5 analysis (Table 13-51(h): p<0.017). Degreasing chemical exposure also was significant in the Model 5 analysis. Appendix Table I-2-36 presents adjusted results stratified by age for Model 5. When the current dioxin-by-age interaction was removed from Model 5, the adjusted analysis found a significant positive association between apolipoprotein B and current dioxin (Table 13-51(h): p<0.001, Adj. Slope=0.0246). After adjusting for age, lifetime alcohol history, and degreasing chemical exposure, the adjusted Model 6 analysis did not disclose a significant association between apolipoprotein B and current dioxin (Table 13-51(h): p=0.581).

Apolipoprotein B (Discrete)

The unadjusted and adjusted Model 1 analyses did not find a significant group difference in the percentage of individuals having high apolipoprotein B levels (Table 13-52(a,b): p>0.26 for all contrasts). The adjusted Model 1 analysis contained two interactions: age-by-lifetime alcohol history and occupation-by-race.

The unadjusted Model 2 results did not show a significant association between apolipoprotein B and initial dioxin (Table 13-52(c): p=0.310). Initial dioxin-by-age was a significant interaction in the adjusted Model 2 analysis (Table 13-52(d): p=0.024). Appendix Table I-2-37 presents adjusted results stratified by age. In addition to the initial dioxin-by-age interaction, the final model also included occupation and degreasing chemical exposure. The adjusted Model 2 analysis did not detect a significant association between apolipoprotein B and initial dioxin when the initial dioxin-by-age interaction was removed from the final model (Table 13-52(d): p=0.605).

Examination of the unadjusted Model 3 results revealed a marginally significant difference between the high Ranch Hands and the Comparison group in the percentage of individuals with high apolipoprotein B levels (Table 13-52(e): p=0.058, Est. RR=1.37, 95% C.I.=[0.99, 1.90]). The percentage of apolipoprotein B abnormalities was higher for the high Ranch Hands than for the Comparisons (77.9% vs. 71.8%). All other contrasts involving the Comparisons were nonsignificant.

After adjusting for covariates in the Model 3 analysis, the contrast between the high Ranch Hands and Comparisons became nonsignificant (Table 13-52(f): p=0.141). All other contrasts involving the Comparisons remained nonsignificant in the adjusted analysis. The

Table 13-52.
Analysis of Apolipoprotein B
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent High**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***939***	***73.9***	***1.09 (0.90,1.32)***	***0.384***
	Comparison	***1,253***	***72.1***		
Officer	Ranch Hand	361	70.4	1.06 (0.79,1.43)	0.746
	Comparison	495	69.1		
Enlisted Flyer	Ranch Hand	162	79.6	0.85 (0.50,1.44)	0.640
	Comparison	196	82.1		
Enlisted Groundcrew	Ranch Hand	416	74.8	1.19 (0.89,1.58)	0.266
	Comparison	562	71.4		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.05 (0.87,1.28)***	***0.597***	AGE*DRKYR (p=0.010) OCC*RACE (p=0.034)
Officer	1.04 (0.77,1.40)	0.789	
Enlisted Flyer	0.79 (0.46,1.34)	0.376	
Enlisted Groundcrew	1.16 (0.87,1.55)	0.311	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 13-52. (Continued)
Analysis of Apolipoprotein B
(Discrete)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	173	74.6	1.08 (0.93,1.26)	0.310
Medium	170	75.3		
High	172	76.2		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
515	1.05 (0.87,1.26)**	0.605**	INIT*AGE (p=0.024) OCC (p=0.108) DC (p=0.098)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-37 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 13-52. (Continued)
Analysis of Apolipoprotein B
(Discrete)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	**n**	**Percent High**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,043	71.8		
Background RH	369	71.3	0.98 (0.75,1.28)	0.890
Low RH	257	72.8	1.06 (0.78,1.44)	0.719
High RH	258	77.9	1.37 (0.99,1.90)	0.058
Low plus High RH	515	75.3	1.20 (0.94,1.53)	0.146

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	**n**	**Adj. Relative Risk (95% C.I.)[ac]**	**p-Value**	**Covariate Remarks**
Comparison	1,025			ALC (p=0.058) OCC*RACE (p=0.035) AGE*DRKYR (p=0.029)
Background RH	362	1.02 (0.77,1.34)	0.915	
Low RH	251	0.99 (0.72,1.35)	0.950	
High RH	251	1.29 (0.92,1.82)	0.141	
Low plus High RH	502	1.12 (0.87,1.44)	0.376	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 13-52. (Continued)
Analysis of Apolipoprotein B
(Discrete)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent High/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	71.0 (290)	72.5 (298)	77.4 (296)	1.09 (0.98,1.21)	0.100
5	67.7 (294)	75.4 (297)	77.8 (293)	1.16 (1.06,1.27)	0.001
6[c]	67.6 (293)	75.4 (297)	77.8 (293)	0.98 (0.89,1.09)	0.719

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	884	1.09 (0.98,1.21)	0.100	
5	884	1.17 (1.07,1.28)**	<0.001**	CURR*AGE (p=0.019)
6[c]	883	0.98 (0.89,1.09)	0.719	

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

** Log_2 (current dioxin + 1)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and
p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-37 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

adjusted Model 3 analysis contained current alcohol use and two interactions: occupation-by-race and age-by-lifetime alcohol history.

Removing occupation from the adjusted analysis produced a change in the adjusted results. The adjusted Model 3 analysis showed the high Ranch Hands to be significantly different from the Comparisons when occupation was removed from the final model (Appendix Table I-3-39(b): p=0.038, Adj. RR=1.42, 95% C.I.=[1.02, 1.98]).

The unadjusted Model 4 analysis detected a marginally significant association between apolipoprotein B and current dioxin (Table 13-52(g): p=0.100, Est. RR=1.09, 95% C.I.=[0.98, 1.21]). The unadjusted and adjusted Model 4 results were identical because no covariates were retained in the adjusted Model 4 analysis.

The unadjusted Model 5 results revealed a significant association between apolipoprotein B and current dioxin (Table 13-52(g): p=0.001, Est. RR=1.16, 95% C.I.=[1.06, 1.27]). Current dioxin-by-age was a significant interaction in the adjusted Model 5 analysis (Table 13-52(h): p=0.019). Appendix Table I-2-37(b) presents adjusted results stratified by age. When the current dioxin-by-age interaction was removed from the adjusted Model 5 analysis, the association between apolipoprotein B and current dioxin remained significant in the adjusted analysis (Table 13-52(h): p<0.001, Adj. RR=1.17, 95% C.I.=[1.07, 1.28]).

The unadjusted and adjusted Model 6 analyses did not reveal a significant association between apolipoprotein B and current dioxin (Table 13-52(g,h): p=0.719 for both analyses). No covariates were retained in the adjusted Model 6 analysis.

C_3 Complement (Continuous)

The unadjusted and adjusted Model 1 analyses did not reveal a significant group difference in the mean levels of C_3 complement (Table 13-53(a,b): p>0.15 for all analyses). Age, race, occupation, current alcohol use, and degreasing chemical exposure were significant covariates in the adjusted Model 1 analysis.

The unadjusted Model 2 results revealed a significant positive association between C_3 complement and initial dioxin (Table 13-53(c): p=0.041, Est. Slope=0.0099). The adjusted Model 2 analysis also detected a significant positive association between C_3 complement and initial dioxin (Table 13-53(d): p=0.031, Adj. Slope=0.0105). The final model contained the covariates race and current alcohol use.

The unadjusted Model 3 analysis showed that the background Ranch Hand category had a significantly lower mean C_3 complement than the Comparison group (Table 13-53(e): p=0.004), while the high Ranch Hand category and the low plus high Ranch Hand category had marginally higher means than the Comparison group (Table 13-53(e): p=0.068 and p=0.051). The means, adjusted for percent body fat at the time of duty in SEA and the change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, were 114.40 mg/dl, 111.53 mg/dl, 115.79 mg/dl, 116.53 mg/dl, and 116.16 mg/dl for the Comparison group, the background Ranch Hand category, the low Ranch Hand

Table 13-53.
Analysis of C_3 Complement (mg/dl)
(Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Mean[a]**	**Difference of Means (95% C.I.)[b]**	**p-Value[c]**
All	*Ranch Hand*	*939*	*114.14*	*-0.22 --*	*0.773*
	Comparison	*1,253*	*114.36*		
Officer	Ranch Hand	361	111.52	0.45 --	0.690
	Comparison	495	111.07		
Enlisted Flyer	Ranch Hand	162	114.35	-2.05 --	0.298
	Comparison	196	116.40		
Enlisted Groundcrew	Ranch Hand	416	116.39	-0.23 --	0.840
	Comparison	562	116.62		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED						
Occupational Category	**Group**	**n**	**Adj. Mean[a]**	**Difference of Adj. Means (95% C.I.)[b]**	**p-Value[c]**	**Covariate Remarks[d]**
All	*Ranch Hand*	*929*	*116.09*	*-0.43 --*	*0.566*	AGE ($p<0.001$)
	Comparison	*1,235*	*116.52*			RACE ($p=0.001$)
Officer	Ranch Hand	361	113.58	0.64 --	0.588	OCC ($p<0.001$)
	Comparison	488	112.94			ALC ($p=0.042$)
						DC ($p=0.035$)
Enlisted Flyer	Ranch Hand	159	115.38	-2.65 --	0.157	
	Comparison	196	118.03			
Enlisted Groundcrew	Ranch Hand	409	118.63	-0.59 --	0.612	
	Comparison	551	119.22			

[a] Transformed from natural logarithm scale.

[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

[c] P-values based on difference of means on natural logarithm scale.

[d] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 13-53. (Continued)
Analysis of C_3 Complement (mg/dl)
(Continuous)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	173	114.89	115.40	0.074	0.0099 (0.0048)	0.041
Medium	170	116.69	116.81			
High	172	119.80	119.15			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[d]			
Initial Dioxin	n	Adj. Mean[ad]	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
Low	171	118.56	0.090	0.0105 (0.0049)	0.031	RACE (p=0.012) ALC (p=0.129)
Medium	167	120.23				
High	170	122.63				

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Slope and standard error based on natural logarithm of C_3 complement versus $\log_2$ (initial dioxin).

[d] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 13-53. (Continued)
Analysis of C_3 Complement (mg/dl)
(Continuous)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED					
Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,043	114.46	114.40		
Background RH	369	110.12	111.53	-2.87 --	0.004
Low RH	257	116.22	115.79	1.39 --	0.233
High RH	258	118.00	116.53	2.13 --	0.068
Low plus High RH	515	117.11	116.16	1.76 --	0.051

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED					
Dioxin Category	n	Adj. Mean[ae]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]	Covariate Remarks
Comparison	1,043	116.25			AGE (p<0.001) RACE (p=0.007) OCC (p<0.001) DC (p=0.089)
Background RH	369	114.16	-2.09 --	0.043	
Low RH	257	117.32	1.07 --	0.361	
High RH	258	117.42	1.17 --	0.335	
Low plus High RH	515	117.37	1.12 --	0.223	

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not presented because analysis was performed on natural logarithm scale.

[d] P-value is based on difference of means on natural logarithm scale.

[e] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 13-53. (Continued)
Analysis of C_3 Complement (mg/dl)
(Continuous)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED						
	Current Dioxin Category Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)		
Model[b]	Low	Medium	High	R^2	Slope (Std. Error)[c]	p-Value
4	109.86 (290)	114.47 (298)	118.15 (296)	0.051	0.0232 (0.0034)	<0.001
5	109.35 (294)	114.27 (297)	119.02 (293)	0.073	0.0240 (0.0029)	<0.001
6[d]	111.14 (293)	114.43 (297)	117.05 (293)	0.119	0.0160 (0.0030)	<0.001

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED							
	Current Dioxin Category Adjusted Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)			
Model[b]	Low	Medium	High	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
4	111.84 (287)	115.71 (290)	119.83 (287)	0.077	0.0233 (0.0039)	<0.001	AGE (p=0.018) RACE (p=0.028) OCC*IC (p=0.030) DRKYR*IC (p=0.042)
5	111.67** (294)	116.15** (297)	121.34** (293)	0.102	0.0245 (0.0032)**	<0.001**	CURR*OCC (p=0.031) AGE (p=0.069) RACE (p=0.009) OCC*IC (p=0.037)
6[e]	113.86 (289)	116.37 (290)	119.27 (284)	0.149	0.0154 (0.0034)	<0.001	AGE (p=0.076) RACE (p=0.005) OCC*IC (p=0.013) DRKYR*IC (p=0.029)

[a] Transformed from natural logarithm scale.

[b] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[c] Slope and standard error based on natural logarithm of C_3 complement versus log_2 (current dioxin + 1).

[d] Adjusted for log_2 total lipids.

[e] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-38 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

category, the high Ranch Hand category, and the low plus high Ranch hand category respectively.

After adjusting for the covariates age, race, occupation, and degreasing chemical exposure, the background Ranch Hand mean C_3 complement remained significantly lower than the Comparison group mean (Table 13-53(f): p=0.043, 114.16 mg/dl versus 116.25 mg/dl), but the high versus Comparison group contrast and the low plus high versus Comparison group contrast became nonsignificant ($p>0.22$ for both contrasts). The change in significance for the high versus Comparison contrast and the low plus high versus Comparison contrast was due to adjusting for occupation. After excluding occupation from the final model, the adjusted results paralleled the unadjusted findings, showing marginally significant mean differences for both these contrasts (Appendix Table I-3-40(a): p=0.069 for the high versus Comparison contrast and p=0.077 for the low plus high versus Comparison contrast).

The unadjusted analyses for Models 4, 5, and 6 revealed a significant positive association between C_3 complement and current dioxin (Table 13-53(g): $p<0.001$, Est. Slope=0.0232; $p<0.001$, Est. Slope=0.0240; and $p<0.001$, Est. Slope=0.0160 respectively). For Models 4 and 6, each of the adjusted analyses also detected a significant positive association between C_3 complement and current dioxin (Table 13-53(h): $p<0.001$, Adj. Slope=0.0233 and $p<0.001$, Adj. Slope=0.0154 respectively). Each of the adjusted analyses for Models 4 and 6 contained age, race, and two interactions: occupation-by-industrial chemical exposure and lifetime alcohol history-by-industrial chemical exposure.

Current dioxin-by-occupation was a significant interaction in the adjusted Model 5 analysis (Table 13-53(h): p=0.031). Appendix Table I-2-38(a) presents adjusted results stratified by occupation for Model 5. In addition to the current dioxin-by-occupation interaction, the adjusted Model 5 analysis contained age, race, and the occupation-by-industrial chemical exposure interaction. After removing the current dioxin-by-occupation interaction from the final model, the association between C_3 complement and current dioxin remained significant in the adjusted Model 5 analysis (Table 13-53(h): $p<0.001$, Adj. Slope=0.0245).

C_3 Complement (Discrete)

The unadjusted Model 1 analysis did not show a significant group difference in the percentage of participants having low levels of C_3 complement (Table 13-54(a): $p>0.26$ for all contrasts). The interaction between group and race was significant in the adjusted Model 1 analysis (Table 13-54(b): p=0.021). Appendix Table I-2-39 presents adjusted results stratified by race. The final model also contained two other interactions: occupation-by-lifetime alcohol history and current alcohol use-by-industrial chemical exposure. The adjusted analysis did not show a significant group contrast when the group-by-race interaction was removed from the final model (Table 13-54(b): $p>0.13$ for all contrasts).

The unadjusted and adjusted Model 2 analyses did not reveal a significant association between C_3 complement and initial dioxin (Table 13-54(c,d): $p>0.33$ for both analyses). The

Table 13-54.
Analysis of C_3 Complement
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Low**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	*Ranch Hand*	*939*	*2.6*	*1.07 (0.62,1.84)*	*0.918*
	Comparison	*1,253*	*2.4*		
Officer	Ranch Hand	361	2.8	0.85 (0.38,1.90)	0.851
	Comparison	495	3.2		
Enlisted Flyer	Ranch Hand	162	2.5	0.68 (0.20,2.38)	0.769
	Comparison	196	3.6		
Enlisted Groundcrew	Ranch Hand	416	2.4	1.95 (0.74,5.17)	0.261
	Comparison	562	1.2		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	*1.10 (0.64,1.90)***	*0.734***	GROUP*RACE (p=0.021) OCC*DRKYR (p=0.039) ALC*IC (p=0.016)
Officer	0.86 (0.38,1.91)**	0.704**	
Enlisted Flyer	0.71 (0.20,2.49)**	0.594**	
Enlisted Groundcrew	2.14 (0.79,5.84)**	0.137**	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

** Group-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-39 for further analysis of this interaction.

Table 13-54. (Continued)
Analysis of C_3 Complement
(Discrete)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Low	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	173	1.2	0.83 (0.47,1.46)	0.504
Medium	170	2.4		
High	172	1.2		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
508	0.74 (0.39,1.41)	0.337	RACE (p=0.103) IC (p=0.039) DC (p=0.061) ALC (p=0.024)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 13-54. (Continued)
Analysis of C_3 Complement
(Discrete)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	**n**	**Percent Low**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,043	2.7		
Background RH	369	3.8	1.23 (0.63,2.38)	0.549
Low RH	257	1.9	0.72 (0.27,1.90)	0.504
High RH	258	1.2	0.46 (0.13,1.55)	0.210
Low plus High RH	515	1.6	0.59 (0.26,1.33)	0.207

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	**n**	**Adj. Relative Risk (95% C.I.)[ac]**	**p-Value**	**Covariate Remarks**
Comparison	1,027			DXCAT*RACE (p=0.028) DXCAT*IC (p=0.003) IC*DC (p=0.021) IC*ALC (p<0.001)
Background RH	367	1.25 (0.63,2.46)**	0.520**	
Low RH	254	0.74 (0.28,1.97)**	0.544**	
High RH	254	0.40 (0.12,1.37)**	0.144**	
Low plus High RH	508	0.56 (0.25,1.28)**	0.169**	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interaction ($p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-39 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 13-54. (Continued)
Analysis of C_3 Complement
(Discrete)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Low/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	3.4 (290)	2.3 (298)	1.7 (296)	0.68 (0.49,0.94)	0.014
5	4.4 (294)	2.0 (297)	1.0 (293)	0.70 (0.56,0.87)	0.003
6[c]	4.1 (293)	2.0 (297)	1.0 (293)	0.86 (0.65,1.13)	0.282

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	875	0.68 (0.47,0.97)**	0.032**	CURR*ALC (p=0.011) DC (p=0.075) OCC*AGE (p=0.037)
5	875	0.66 (0.51,0.85)	0.003	DC (p=0.052) OCC*AGE (p=0.022) IC*ALC (p=0.032)
6[d]	874	0.85 (0.62,1.17)	0.330	DC (p=0.051) OCC*AGE (p=0.011) IC*ALC (p=0.032)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-39 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

adjusted Model 2 analysis included race, industrial chemical exposure, degreasing chemical exposure, and current alcohol use.

Examination of the unadjusted Model 3 results did not show a significant contrast between any of the Ranch Hand categories and the Comparison group (Table 13-54(e): $p>0.20$ for all contrasts). Categorized dioxin-by-race and categorized dioxin-by-industrial chemical exposure were significant interactions in the adjusted Model 3 analysis. Appendix Table I-2-39(b,c) presents adjusted results stratified separately by race and industrial chemical exposure. The final model also included two covariate-by-covariate interactions: industrial chemical exposure-by-degreasing chemical exposure and industrial chemical exposure-by-current alcohol use. The adjusted Model 3 analysis did not detect a significant difference between any of the Ranch Hand categories and the Comparison group when the two categorized dioxin-by-covariate interactions were removed from the final model (Table 13-54(f): $p>0.14$ for all contrasts).

The unadjusted analyses for Models 4 and 5 detected a significant inverse association between low levels of C_3 complement and current dioxin (Table 13-54(g): p=0.014, Est. RR=0.68, 95% C.I.=[0.49, 0.94] and p=0.003, Est. RR=0.70, 95% C.I.=[0.56, 0.87] for Models 4 and 5 respectively). By contrast, the unadjusted Model 6 analysis did not show a significant association (Table 13-54(g): p=0.282).

Current dioxin-by-current alcohol use was a significant interaction in the adjusted Model 4 analysis. Appendix Table I-2-39 presents adjusted results stratified by current alcohol use for Model 4. The adjusted Model 4 analysis also included degreasing chemical exposure and the occupation-by-age interaction. After removing the current dioxin-by-current alcohol use interaction from the final model, the association between C_3 complement and current dioxin remained significant (Table 13-54(h): p=0.032, Adj. RR=0.68, 95% C.I.=[0.47, 0.97]).

The adjusted results for Models 5 and 6 corresponded to the unadjusted results for these models. The adjusted Model 5 analysis found a significant inverse association between C_3 complement and current dioxin (Table 13-54(h): p=0.003, Adj. RR=0.66, 95% C.I.=[0.51, 0.85]), but the Model 6 adjusted analysis did not find a significant association (Table 13-54(h): p=0.330).

These seemingly discrepant results for C_3 complement (in continuous analyses, significantly increasing abnormally low levels as dioxin increases and, in discrete analyses, significantly decreasing abnormally low levels as dioxin increases) are consistent because low levels of C_3 are considered abnormal in the discrete analyses results.

C_4 Complement (Continuous)

The unadjusted and adjusted Model 1 analyses did not show a significant group difference in the mean levels of C_4 complement (Table 13-55(a,b): $p>0.51$ for all contrasts). The adjusted analysis contained age, race, occupation, lifetime alcohol history, and industrial chemical exposure.

Table 13-55.
Analysis of C_4 Complement (mg/dl)
(Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	*Ranch Hand*	*939*	*21.73*	*-0.07 --*	*0.763*
	Comparison	*1,253*	*21.80*		
Officer	Ranch Hand	361	21.15	-0.13 --	0.711
	Comparison	495	21.28		
Enlisted Flyer	Ranch Hand	162	22.21	0.36 --	0.565
	Comparison	196	21.85		
Enlisted Groundcrew	Ranch Hand	416	22.07	-0.19 --	0.573
	Comparison	562	22.25		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]	Covariate Remarks[d]
All	*Ranch Hand*	*917*	*23.17*	*-0.12 --*	*0.617*	AGE (p=0.027)
	Comparison	*1,232*	*23.29*			RACE (p<0.001)
Officer	Ranch Hand	357	22.66	-0.19 --	0.619	OCC (p=0.008) DRKYR (p=0.126)
	Comparison	487	22.84			IC (p=0.131)
Enlisted Flyer	Ranch Hand	156	23.49	0.36 --	0.548	
	Comparison	195	23.13			
Enlisted Groundcrew	Ranch Hand	404	23.56	-0.24 --	0.515	
	Comparison	550	23.80			

[a] Transformed from natural logarithm scale.

[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

[c] P-values based on difference of means on natural logarithm scale.

[d] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 13-55. (Continued)
Analysis of C_4 Complement (mg/dl)
(Continuous)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	173	21.40	21.45	0.008	0.0020 (0.0083)	0.814
Medium	170	22.15	22.16			
High	172	22.17	22.11			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[d]			
Initial Dioxin	n	Adj. Mean[ad]	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
Low	171	22.40**	0.088	0.0020 (0.0097)**	0.834**	INIT*OCC (p=0.002) INIT*AGE (p=0.027)
Medium	167	23.35**				RACE (p=0.014) OCC*ALC (p=0.014)
High	170	23.24**				OCC*IC (p=0.007)

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Slope and standard error based on natural logarithm of C_4 complement versus $\log_2$ (initial dioxin).

[d] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interaction ($p \leq 0.05$); adjusted mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-40 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 13-55. (Continued)
Analysis of C_4 Complement (mg/dl)
(Continuous)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED					
Dioxin Category	**n**	**Mean[a]**	**Adj. Mean[ab]**	**Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]**	**p-Value[d]**
Comparison	1,043	21.76	21.76		
Background RH	369	21.32	21.46	-0.30 --	0.347
Low RH	257	21.97	21.94	0.18 --	0.619
High RH	258	21.83	21.69	-0.07 --	0.857
Low plus High RH	515	21.90	21.82	0.06 --	0.838

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED					
Dioxin Category	**n**	**Adj. Mean[ae]**	**Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]**	**p-Value[d]**	**Covariate Remarks**
Comparison	1,025	23.06			AGE (p=0.053) RACE (p<0.001) OCC (p=0.014) DRKYR (p=0.063)
Background RH	362	22.85	-0.20 --	0.554	
Low RH	251	23.17	0.11 --	0.772	
High RH	251	22.78	-0.28 --	0.487	
Low plus High RH	502	22.98	-0.08 --	0.785	

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not presented because analysis was performed on natural logarithm scale.

[d] P-value is based on difference of means on natural logarithm scale.

[e] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 13-55. (Continued)
Analysis of C_4 Complement (mg/dl)
(Continuous)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED						
	Current Dioxin Category Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)		
Model[b]	Low	Medium	High	R^2	Slope (Std. Error)[c]	p-Value
4	21.16 (290)	21.82 (298)	22.00 (296)	0.004	0.0102 (0.0056)	0.068
5	21.03 (294)	21.69 (297)	22.27 (293)	0.009	0.0138 (0.0048)	0.004
6[d]	21.44 (293)	21.73 (297)	21.83 (293)	0.041	0.0038 (0.0051)	0.452

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED							
	Current Dioxin Category Adjusted Mean[a]/(n)			Analysis Results for Log_2 (Current Dioxin + 1)			
Model[b]	Low	Medium	High	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
4	22.31 (287)	22.84 (290)	22.78 (287)	0.046	0.0071 (0.0064)	0.267	RACE (p=0.002) OCC*ALC (p=0.035) OCC*IC (p=0.009) ALC*DRKYR (p=0.041)
5	22.19** (290)	22.66** (290)	23.27** (284)	0.058	0.0129 (0.0054)**	0.018**	CURR*OCC (p=0.031) RACE (p=0.002) OCC*ALC (p=0.030) OCC*IC (p=0.009) ALC*DRKYR (p=0.041)
6[e]	22.82 (289)	22.80 (290)	22.86 (284)	0.078	0.0006 (0.0058)	0.920	RACE (p<0.001) OCC*IC (p=0.004) ALC*DRKYR (p=0.036)

[a] Transformed from natural logarithm scale.

[b] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[c] Slope and standard error based on natural logarithm of C_4 complement versus log_2 (current dioxin + 1).

[d] Adjusted for log_2 total lipids.

[e] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-40 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Examination of the unadjusted Model 2 results did not reveal a significant association between C_4 complement and initial dioxin (Table 13-55(c): $p=0.814$). Initial dioxin-by-occupation and initial dioxin-by-age were significant interactions in the adjusted analysis of Model 2 (Table 13-55(d): $p=0.002$ and $p=0.027$ respectively). Appendix Table I-2-40(a,b) presents adjusted results stratified separately by age and occupation. The final model also included race and two covariate-by-covariate interactions: occupation-by-current alcohol use and occupation-by-industrial chemical exposure. When the two initial dioxin-by-covariate interactions were removed from the final model, the association between C_4 complement and initial dioxin remained nonsignificant (Table 13-55(d): $p=0.834$).

The unadjusted and adjusted Model 3 analyses did not show any of the Ranch Hand categories to be significantly different from the Comparison group (Table 13-55(e,f): $p>0.34$ for all contrasts). Age, race, occupation, and lifetime alcohol history were significant covariates in the adjusted analysis.

The unadjusted analyses for Models 4 and 5 detected a marginally significant and significant positive association between C_4 complement and current dioxin (Table 13-55(g): $p=0.068$, Est. Slope=0.0102 and $p=0.004$, Est. Slope=0.0138 respectively). The Model 6 analysis did not show a significant association (Table 13-55(g): $p=0.452$).

After covariate adjustment, the association between C_4 complement and current dioxin became nonsignificant in the Model 4 analysis (Table 13-55(h): $p=0.267$). The adjusted Model 4 analysis contained race and three covariate-by-covariate interactions: occupation-by-current alcohol use, occupation-by-industrial chemical exposure, and current alcohol use-by-lifetime alcohol history).

The adjusted Model 4 results corresponded to the unadjusted results when occupation was removed from the final model. This adjusted analysis detected a marginally significant association between C_4 complement and current dioxin (Appendix Table I-3-42(c): $p=0.080$, Adj. Slope=0.0100).

Current dioxin-by-occupation was a significant interaction in the adjusted analysis of Model 5 (Table 13-55(h): $p=0.031$). Appendix Table I-2-40 presents adjusted results stratified by occupation. In addition to this interaction, the final model also included race and three covariate-by-covariate interactions: occupation-by-current alcohol use, occupation-by-industrial chemical exposure, and current alcohol use-by-lifetime alcohol history. The association between C_4 complement and current dioxin remained significant after the current dioxin-by-occupation interaction was removed from the adjusted Model 5 analysis (Table 13-55(h): $p=0.018$, Adj. Slope=0.0129).

The adjusted Model 6 analysis did not reveal a significant association between C_4 complement and current dioxin (Table 13-55(h): $p=0.920$). The final model contained race and two covariate-by-covariate interactions: occupation-by-industrial chemical exposure and current alcohol use-by-lifetime alcohol history.

C_4 Complement (Discrete)

The unadjusted and adjusted Model 1 analyses did not reveal a significant group difference in the percentage of participants having low C_4 complement levels (Table 13-56(a,b): $p>0.17$ for all contrasts). The final adjusted model contained occupation and current alcohol use.

The unadjusted and adjusted Model 2 results did not show a significant association between C_4 complement and initial dioxin (Table 13-56(c,d): $p>0.64$ for both analyses). Lifetime alcohol history was the only covariate in the final model.

Examination of the unadjusted and adjusted Model 3 results did not reveal a significant difference between any of the Ranch Hand categories and the Comparison group (Table 13-56(e,f): $p>0.53$ for all contrasts). The final model contained occupation and current alcohol.

The unadjusted and adjusted analyses for Models 4 through 6 did not show a significant association between C_4 complement and current dioxin (Table 13-56(g,h): $p>0.42$ for all analyses). Lifetime alcohol history was the only covariate in each of the adjusted analyses.

Haptoglobin (Continuous)

The unadjusted Model 1 analysis revealed a significant overall group difference in the mean levels of haptoglobin (Table 13-57(a): $p=0.004$). The mean level of haptoglobin was higher for the Ranch Hands than for Comparisons (114.81 mg/dl vs. 109.17 mg/dl). Stratifying the unadjusted analysis by occupation uncovered a significant group difference within the enlisted groundcrew stratum ($p=0.015$). For the enlisted groundcrew, the mean level of haptoglobin was higher for the Ranch Hands than for the Comparisons (119.29 mg/dl vs. 112.20 mg/dl).

After covariate adjustment, the overall group contrast remained significant (Table 13-57(b): $p=0.016$). Similarly, the enlisted groundcrew group contrast remained significant when the adjusted Model 1 analysis was stratified by occupation ($p=0.034$). The final model contained race, occupation, and four covariate-by-covariate interactions: age-by-lifetime alcohol history, lifetime alcohol history-by-current alcohol use, current alcohol use-by-industrial chemical exposure, and current alcohol use-by-degreasing chemical exposure.

The unadjusted Model 2 results did not reveal a significant association between haptoglobin and initial dioxin (Table 13-57(c): $p=0.326$). Initial dioxin-by-age and initial dioxin-by-lifetime alcohol history were significant interactions in the adjusted Model 2 analysis (Table 13-57(d): $p=0.016$ and $p=0.023$ respectively). Appendix Table I-2-41 presents adjusted results stratified separately by age and lifetime alcohol history. The final model also included race and the age-by-occupation interaction. The adjusted analysis did not show a significant association between haptoglobin and initial dioxin when the two initial dioxin-by-covariate interactions were removed from the final model (Table 13-57(d): $p=0.452$).

Table 13-56.
Analysis of C_4 Complement
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Low**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	*Ranch Hand*	*939*	*0.6*	*0.89 (0.32,2.51)*	*0.999*
	Comparison	*1,253*	*0.7*		
Officer	Ranch Hand	361	0.8	1.37 (0.28,6.85)	0.999
	Comparison	495	0.6		
Enlisted Flyer	Ranch Hand	162	0.6	0.24 (0.03,2.05)	0.315
	Comparison	196	2.6		
Enlisted Groundcrew	Ranch Hand	416	0.5	2.71 (0.24,29.99)	0.793
	Comparison	562	0.2		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	*0.86 (0.30,2.44)*	*0.775*	OCC (p=0.037) ALC (p=0.111)
Officer	1.41 (0.28,7.02)	0.677	
Enlisted Flyer	0.23 (0.03,1.95)	0.177	
Enlisted Groundcrew	2.73 (0.24,30.55)	0.415	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 13-56. (Continued)
Analysis of C_4 Complement
(Discrete)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Low	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	173	0.0	1.20 (0.56,2.58)	0.644
Medium	170	1.2		
High	172	0.6		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
502	1.18 (0.52,2.65)	0.695	DRKYR (p=0.118)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 13-56. (Continued)
Analysis of C_4 Complement
(Discrete)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent Low	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,043	0.8		
Background RH	369	0.8	1.00 (0.26,3.85)	0.997
Low RH	257	0.8	0.98 (0.20,4.66)	0.977
High RH	258	0.4	0.51 (0.06,4.17)	0.530
Low plus High RH	515	0.6	0.75 (0.20,2.88)	0.676

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,027			OCC (p=0.117) ALC (p=0.120)
Background RH	367	0.96 (0.24,3.78)	0.954	
Low RH	254	0.85 (0.17,4.11)	0.838	
High RH	254	0.55 (0.06,4.75)	0.585	
Low plus High RH	508	0.72 (0.18,2.87)	0.644	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 13-56. (Continued)
Analysis of C_4 Complement
(Discrete)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Low/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	1.0 (290)	0.3 (298)	0.7 (296)	0.86 (0.48,1.54)	0.608
5	1.0 (294)	0.7 (297)	0.3 (293)	0.83 (0.53,1.31)	0.430
6[c]	1.0 (293)	0.7 (297)	0.3 (293)	0.94 (0.56,1.56)	0.808

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	864	0.86 (0.48,1.53)	0.595	DRKYR (p=0.099)
5	864	0.82 (0.51,1.32)	0.421	DRKYR (p=0.098)
6[d]	863	0.91 (0.54,1.54)	0.732	DRKYR (p=0.129)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 13-57.
Analysis of Haptoglobin (mg/dl)
(Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Mean**	**Difference of Means (95% C.I.)**	**p-Value**
All	*Ranch Hand*	*939*	*114.81*	*5.64 (1.77,9.51)*	*0.004*
	Comparison	*1,253*	*109.17*		
Officer	Ranch Hand	361	105.72	3.75 (-2.19,9.69)	0.216
	Comparison	495	101.97		
Enlisted Flyer	Ranch Hand	162	123.56	4.89 (-5.38,15.16)	0.351
	Comparison	196	118.67		
Enlisted Groundcrew	Ranch Hand	416	119.29	7.09 (1.37,12.80)	0.015
	Comparison	562	112.20		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED						
Occupational Category	**Group**	**n**	**Adj. Mean**	**Difference of Adj. Means (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	*Ranch Hand*	*917*	*110.05*	*4.69 (0.88,8.50)*	*0.016*	RACE (p=0.011)
	Comparison	*1,232*	*105.36*			OCC (p<0.001)
Officer	Ranch Hand	357	97.01	3.45 (-2.65,9.55)	0.267	AGE*DRKYR (p=0.016)
	Comparison	487	93.56			DRKYR*ALC (p=0.001)
						ALC*IC (p=0.039)
Enlisted Flyer	Ranch Hand	156	115.13	3.56 (-5.84,12.97)	0.458	ALC*DC (p=0.032)
	Comparison	195	111.57			
Enlisted Groundcrew	Ranch Hand	404	117.54	6.20 (0.47,11.93)	0.034	
	Comparison	550	111.35			

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 13-57. (Continued)
Analysis of Haptoglobin (mg/dl)
(Continuous)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				**Analysis Results for Log_2 (Initial Dioxin)[a]**		
Initial Dioxin	**n**	**Mean**	**Adj. Mean[a]**	**R^2**	**Slope (Std. Error)**	**p-Value**
Low	173	109.58	109.89	0.006	1.4844 (1.5109)	0.326
Medium	170	118.71	118.80			
High	172	119.34	118.94			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)[b]**			
Initial Dioxin	**n**	**Adj. Mean[b]**	**R^2**	**Adj. Slope (Std. Error)**	**p-Value**	**Covariate Remarks**
Low	170	100.74**	0.087	-1.3155 (1.7467)**	0.452**	INIT*AGE (p=0.016) INIT*DRKYR (p=0.023) RACE (p=0.025) AGE*OCC (p=0.003)
Medium	165	105.94**				
High	167	102.60**				

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted mean, adjusted slope, standard error, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-41 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 13-57. (Continued)
Analysis of Haptoglobin (mg/dl)
(Continuous)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED					
Dioxin Category	**n**	**Mean**	**Adj. Mean[a]**	**Difference of Adj. Mean vs. Comparisons (95% C.I.)**	**p-Value**
Comparison	1,043	109.08	109.08		
Background RH	369	110.88	111.26	2.18 (-3.20,7.56)	0.427
Low RH	257	113.07	112.73	3.65 (-2.49,9.79)	0.244
High RH	258	118.63	118.43	9.35 (3.21,15.50)	0.003
Low plus High RH	515	115.85	115.58	6.50 (1.74,11.26)	0.007

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED					
Dioxin Category	**n**	**Adj. Mean[b]**	**Difference of Adj. Mean vs. Comparisons (95% C.I.)**	**p-Value**	**Covariate Remarks**
Comparison	1,025	103.77			RACE (p=0.006) OCC (p<0.001) AGE*DRKYR (p=0.012) ALC*DRKYR (p<0.001) ALC*IC (p=0.021) ALC*DC (p=0.012)
Background RH	362	109.06	5.29 (-0.12,10.71)	0.056	
Low RH	251	105.79	2.02 (-4.05,8.10)	0.514	
High RH	251	109.06	5.29 (-0.99,11.57)	0.099	
Low plus High RH	502	107.42	3.66 (-1.10,8.41)	0.132	

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 13-57. (Continued)
Analysis of Haptoglobin (mg/dl)
(Continuous)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED						
	Current Dioxin Category Mean/(n)			Analysis Results for Log_2 (Current Dioxin + 1)		
Model[a]	Low	Medium	High	R^2	Slope (Std. Error)	p-Value
4	110.66 (290)	113.40 (298)	117.21 (296)	0.002	1.3757 (1.0196)	0.178
5	111.37 (294)	110.68 (297)	119.32 (293)	0.003	1.3748 (0.8754)	0.117
6[b]	112.56 (293)	110.81 (297)	117.83 (293)	0.010	0.7333 (0.9404)	0.436

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED							
	Current Dioxin Category Adjusted Mean/(n)			Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	Low	Medium	High	R^2	Adj. Slope (Std. Error)	p-Value	Covariate Remarks
4	108.80 (287)	106.90 (290)	105.11 (287)	0.062	-1.3884 (1.1494)	0.227	AGE (p<0.001) RACE (p=0.016) OCC (p<0.001) DRKYR (p=0.036) IC (p=0.042) DC (p=0.042)
5	109.52 (290)	104.40 (290)	108.29 (284)	0.061	-0.9036 (0.9707)	0.352	AGE (p<0.001) RACE (p=0.017) OCC (p<0.001) DRKYR (p=0.037) IC (p=0.042) DC (p=0.041)
6[c]	111.11 (289)	104.98 (290)	107.14 (284)	0.066	-1.5966 (1.0468)	0.128	AGE (p=0.001) RACE (p=0.024) OCC (p<0.001) DRKYR (p=0.046) IC (p=0.044) DC (p=0.053)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Adjusted for log_2 total lipids.

[c] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

The unadjusted Model 3 analysis revealed the high Ranch Hands and the low plus high Ranch Hands to be significantly different from the Comparisons (Table 13-57(e): p=0.003 and p=0.007 respectively). The mean levels of haptoglobin, adjusted for percent body fat at the time of duty in SEA and the change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, for the Comparisons, high Ranch Hands, and low plus high Ranch Hands were 109.08 mg/dl, 118.63 mg/dl, and 115.85 mg/dl respectively.

After adjusting for race, occupation, age-by lifetime alcohol history, current alcohol use-by lifetime alcohol history, current alcohol use-by-industrial chemical exposure, and current alcohol use-by-degreasing chemical exposure, both the background Ranch Hand category mean haptoglobin and the high Ranch Hand category mean haptoglobin were marginally higher than the Comparison group mean (Table 13-57(f): p=0.056 and p=0.099 respectively). The adjusted means were 103.77 mg/dl, 109.06 mg/dl, and 109.06 mg/dl for the Comparison group, the background Ranch Hands and the high Ranch Hands respectively. The low plus high versus Comparison group contrast became nonsignificant after covariate adjustment (p=0.132).

The change in results between the unadjusted and adjusted analyses was primarily due to adjustment for occupation. Removing occupation from the adjusted model led to results consistent with the unadjusted analysis. The high Ranch Hand category versus the Comparison group contrast and the low plus high Ranch Hand category versus the Comparison group contrast were both significant (Appendix Table I-3-44: p=0.003 and p=0.017 respectively), while neither the background Ranch Hand category nor the low Ranch Hand category versus Comparison group contrasts were significant (p>0.37 for both contrasts).

The unadjusted and adjusted analyses for Models 4 through 6 did not reveal a significant association between haptoglobin and current dioxin (Table 13-57(g,h): p>0.11 for all analyses). Each of the adjusted analyses contained age, race, occupation, lifetime alcohol history, industrial chemical exposure, and degreasing chemical exposure.

Haptoglobin (Discrete)

The unadjusted and adjusted Model 1 analyses did not reveal a significant group difference in the percentage of participants having high haptoglobin levels (Table 13-58(a,b): p≥0.11 for all contrasts). The adjusted Model 1 analysis contained age, degreasing chemical exposure, lifetime alcohol history, and the occupation-by-industrial chemical exposure interaction.

Examination of the unadjusted Model 2 results did not reveal a significant association between haptoglobin and initial dioxin (Table 13-58(c): p=0.617). Initial dioxin-by occupation and initial dioxin-by-lifetime alcohol history were significant interactions in the adjusted Model 2 analysis (Table 13-58(d): p=0.024 and p=0.032 respectively). Appendix Table I-2-42 presents adjusted results stratified separately by occupation and lifetime alcohol history. The final model also included race. The adjusted analysis did not show a significant association between haptoglobin and initial dioxin when the two initial dioxin-by-covariate interactions were removed from the final model (p=0.918).

Table 13-58.
Analysis of Haptoglobin
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent High**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	*Ranch Hand*	*939*	*13.5*	*1.24 (0.96,1.61)*	*0.110*
	Comparison	*1,253*	*11.2*		
Officer	Ranch Hand	361	9.7	1.07 (0.67,1.71)	0.856
	Comparison	495	9.1		
Enlisted Flyer	Ranch Hand	162	18.5	1.21 (0.70,2.10)	0.592
	Comparison	196	15.8		
Enlisted Groundcrew	Ranch Hand	416	14.9	1.36 (0.94,1.98)	0.127
	Comparison	562	11.4		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	*1.20 (0.92,1.56)*	*0.181*	AGE (p<0.001) DC (p=0.080) DRKYR (p=0.021) OCC*IC (p=0.006)
Officer	1.10 (0.68,1.77)	0.690	
Enlisted Flyer	1.10 (0.62,1.94)	0.755	
Enlisted Groundcrew	1.32 (0.90,1.93)	0.157	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 13-58. (Continued)
Analysis of Haptoglobin
(Discrete)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent High	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	173	9.2	1.05 (0.87,1.27)	0.617
Medium	170	15.9		
High	172	15.7		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
502	1.01 (0.81,1.27)**	0.918**	INIT*OCC (p=0.024) INIT*DRKYR (p=0.032) RACE (p=0.121)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interactions ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of these interactions; refer to Appendix Table I-2-42 for further analysis of these interactions.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 13-58. (Continued)
Analysis of Haptoglobin
(Discrete)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	n	Percent High	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,043	11.2		
Background RH	369	12.2	1.08 (0.74,1.56)	0.696
Low RH	257	12.1	1.08 (0.71,1.64)	0.730
High RH	258	15.1	1.44 (0.97,2.14)	0.068
Low plus High RH	515	13.6	1.25 (0.91,1.73)	0.164

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,025			AGE (p<0.001) DC (p=0.116) OCC*IC (p=0.035) ALC*DRKYR (p=0.042)
Background RH	362	1.17 (0.80,1.73)	0.417	
Low RH	251	0.93 (0.59,1.45)	0.735	
High RH	251	1.32 (0.87,2.00)	0.196	
Low plus High RH	502	1.11 (0.80,1.55)	0.536	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 13-58. (Continued)
Analysis of Haptoglobin
(Discrete)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent High/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	13.8 (290)	11.1 (298)	14.2 (296)	0.98 (0.86,1.12)	0.800
5	13.9 (294)	9.4 (297)	15.7 (293)	1.00 (0.89,1.12)	0.999
6[c]	14.0 (293)	9.4 (297)	15.7 (293)	0.95 (0.84,1.08)	0.440

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	864	0.88 (0.76,1.03)	0.110	AGE (p=0.021) OCC (p=0.002) DRKYR (p=0.009)
5	864	0.93 (0.82,1.06)	0.288	AGE (p=0.011) OCC (p=0.002) ALC*DRKYR (p=0.033)
6[d]	863	0.87 (0.76,1.00)	0.044	AGE (p=0.027) OCC (p=0.002) DRKYR (p=0.011)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

The unadjusted Model 3 analysis detected a marginally significant difference between the high Ranch Hands and the Comparison group (Table 13-58(e): $p=0.068$, Est. RR=1.44, 95% C.I.=[0.97, 2.14]). The percentages of individuals with high haptoglobin levels was higher for the high Ranch Hands than for the Comparisons (15.1% vs. 11.2%).

After covariate adjustment, the Model 3 analysis did not show any of the Ranch Hand categories to be significantly different from the Comparison group (Table 13-58(f): $p>0.19$ for all contrasts). The adjusted Model 3 analysis contained age, degreasing chemical exposure, and two covariate-by-covariate interactions: occupation-by-industrial chemical exposure and current alcohol use-by-lifetime alcohol history.

When occupation was removed from the final model, the adjusted results matched the unadjusted results. The adjusted analysis found a marginally significant difference between the high Ranch Hand category and the Comparison group after occupation was removed from Model 3 (Appendix Table I-3-45(b): $p=0.065$, Adj. RR=1.47, 95% C.I.=[0.98, 2.22]).

The unadjusted analyses for Models 4 through 6 did not reveal a significant association between haptoglobin and current dioxin (Table 13-58(g): $p>0.44$ for all analyses). For Models 4 and 5, the association between haptoglobin and current dioxin remained nonsignificant in the adjusted analyses (Table 13-58(h): $p>0.11$ for both analyses). However, the Model 6 adjusted analysis revealed a significant association between haptoglobin and current dioxin (Table 13-58(h): $p=0.044$, Adj. RR=0.87, 95% C.I.=[0.76, 1.00]). Models 4 and 6 were adjusted for age, occupation, and lifetime alcohol history. Model 5 was adjusted for age, occupation, and the current alcohol use-by-lifetime alcohol history interaction.

For Model 6, removing occupation changed the adjusted results. Without occupation, the adjusted Model 6 analysis did not show a significant association between haptoglobin and current dioxin (Appendix Table I-3-45(c): $p=0.517$).

Transferrin (Continuous)

The unadjusted Model 1 analysis showed that Ranch Hands had a significantly higher mean level of transferrin than Comparisons (Table 13-59(a): $p=0.042$, 295.29 mg/dl vs. 291.65 mg/dl). Stratifying the unadjusted analysis by occupation revealed a significant group difference within the enlisted groundcrew stratum (Table 13-59(a): $p=0.016$). For the enlisted groundcrew, the mean level of transferrin was higher for Ranch Hands than for Comparisons (Table 13-59(a): 298.92 mg/dl vs. 292.43 mg/dl).

The overall group contrast remained significant in the adjusted Model 1 analysis (Table 13-59(b): $p=0.040$). Similarly, the group contrast for the enlisted groundcrew remained significant in the stratified adjusted analysis (Table 13-59(b): $p=0.031$). The final model contained race, current alcohol use, and three covariate-by-covariate interactions: age-by-occupation, age-by-degreasing chemical exposure, and lifetime alcohol history-by-degreasing chemical exposure.

Table 13-59.
Analysis of Transferrin (mg/dl)
(Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	*Ranch Hand*	*939*	*295.29*	*3.64 --*	*0.042*
	Comparison	*1,253*	*291.65*		
Officer	Ranch Hand	361	292.34	3.35 --	0.231
	Comparison	495	289.00		
Enlisted Flyer	Ranch Hand	162	292.64	-3.53 --	0.443
	Comparison	196	296.18		
Enlisted Groundcrew	Ranch Hand	416	298.92	6.49 --	0.016
	Comparison	562	292.43		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED						
Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]	Covariate Remarks[d]
All	*Ranch Hand*	*917*	*288.88*	*3.60 --*	*0.040*	RACE (p=0.001)
	Comparison	*1,232*	*285.27*			ALC (p=0.077)
Officer	Ranch Hand	357	287.22	4.20 --	0.132	AGE*OCC (p=0.033) AGE*DC (p=0.003)
	Comparison	487	283.03			DRKYR*DC (p=0.023)
Enlisted Flyer	Ranch Hand	156	285.86	-3.52 --	0.417	
	Comparison	195	289.37			
Enlisted Groundcrew	Ranch Hand	404	290.98	5.71 --	0.031	
	Comparison	550	285.27			

[a] Transformed from natural logarithm scale.

[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

[c] P-values based on difference of means on natural logarithm scale.

[d] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 13-59. (Continued)
Analysis of Transferrin (mg/dl)
(Continuous)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	173	296.56	296.63	0.003	0.0047 (0.0045)	0.297
Medium	170	297.61	297.55			
High	172	301.84	301.83			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[d]			
Initial Dioxin	n	Adj. Mean[ad]	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
Low	171	295.51**	0.035	0.0032 (0.0052)**	0.532**	INIT*OCC (p=0.049) INIT*IC (p=0.049) ALC (p=0.054) DC (p=0.136)
Medium	167	294.59**				
High	170	298.77**				

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Slope and standard error based on natural logarithm of transferrin versus log_2 (initial dioxin).

[d] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Log_2 (initial dioxin)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted means, adjusted slope, standard error, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-43 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 13-59. (Continued)
Analysis of Transferrin (mg/dl)
(Continuous)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,043	291.28	291.27		
Background RH	369	291.13	290.82	-0.45 --	0.859
Low RH	257	296.72	297.13	5.86 --	0.044
High RH	258	300.61	300.68	9.40 --	0.001
Low plus High RH	515	298.66	298.90	7.63 --	0.001

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Adj. Mean[ae]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]	Covariate Remarks
Comparison	1,025	286.52			RACE (p=0.023) ALC (p=0.036) AGE*DC (p=0.004) DRKYR*DC (p=0.005)
Background RH	362	287.12	0.60 --	0.812	
Low RH	251	292.58	6.06 --	0.035	
High RH	251	295.17	8.65 --	0.003	
Low plus High RH	502	293.87	7.35 --	0.001	

[a] Transformed from natural logarithm scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not presented because analysis was performed on natural logarithm scale.

[d] P-value is based on difference of means on natural logarithm scale.

[e] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 13-59. (Continued)
Analysis of Transferrin (mg/dl)
(Continuous)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[b]	Current Dioxin Category Mean[a]/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) R^2	Slope (Std. Error)[c]	p-Value
4	291.95 (290)	294.49 (298)	300.03 (296)	0.007	0.0101 (0.0031)	0.001
5	290.61 (294)	294.43 (297)	301.58 (293)	0.018	0.0108 (0.0027)	<0.001
6[d]	292.66 (293)	294.62 (297)	299.36 (293)	0.030	0.0074 (0.0028)	0.009

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[b]	Current Dioxin Category Adjusted Mean[a]/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
4	288.85 (287)	290.57 (290)	294.58 (287)	0.042	0.0090 (0.0036)	0.012	RACE*ALC (p=0.014) OCC*DC (p=0.021) DRKYR*DC (p=0.038)
5	287.59 (290)	290.65 (290)	296.72 (284)	0.047	0.0102 (0.0030)	0.001	RACE*ALC (p=0.015) OCC*DC (p=0.020) DRKYR*DC (p=0.032)
6[e]	290.35 (289)	291.45 (290)	294.80 (284)	0.057	0.0066 (0.0032)	0.040	RACE*ALC (p=0.024) OCC*DC (p=0.013) DRKYR*DC (p=0.031)

[a] Transformed from natural logarithm scale.

[b] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[c] Slope and standard error based on natural logarithm of transferrin versus log_2 (current dioxin + 1).

[d] Adjusted for log_2 total lipids.

[e] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

The unadjusted Model 2 results did not reveal a significant association between transferrin and initial dioxin (Table 13-59(c): $p=0.297$). Initial dioxin-by-occupation and initial dioxin-by-industrial chemical exposure were significant interactions in the adjusted analysis of Model 2 (Table 13-59(d): $p=0.049$ for both interactions). Appendix Table I-2-43 displays adjusted results stratified separately by occupation and industrial chemical exposure. In addition to the two initial dioxin-by-covariate interactions, the final model also included current alcohol use and degreasing chemical exposure. The adjusted Model 2 analysis did not show a significant association between transferrin and current dioxin after the two initial dioxin-by-covariate interactions were removed from the final model (Table 13-59(d): $p=0.532$).

The unadjusted Model 3 analysis showed the low Ranch Hands, high Ranch Hands, and low plus high Ranch Hands to be significantly different from the Comparison group (Table 13-59(e): $p=0.044$, $p=0.001$, and $p=0.001$ respectively). The mean levels of transferrin, adjusted for percent body fat at the time of duty in SEA and the change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, for the Comparisons, low Ranch Hands, high Ranch Hands, and low plus high Ranch Hands were 291.27 mg/dl, 297.13 mg/dl, 300.68 mg/dl, and 298.90 mg/dl respectively.

The adjusted Model 3 result corresponded to the unadjusted results. The adjusted results revealed significant contrasts for the low Ranch Hands, high Ranch Hands, and low plus high Ranch Hands (Table 13-59(f): $p=0.035$, $p=0.003$, and $p=0.001$ respectively). The final model contained race, current alcohol use, and two covariate-by-covariate interactions: age-by-degreasing chemical exposure and lifetime alcohol history-by-degreasing chemical exposure.

Examination of the unadjusted results for Models 4 through 6 revealed a significant association between transferrin and current dioxin for all three models (Table 13-59(g): $p=0.001$, Est. Slope=0.0101; $p<0.001$, Est. Slope=0.0108; and $p=0.009$, Est. Slope=0.0074 for Models 4, 5, and 6 respectively).

The association between transferrin and current dioxin remained significant in each of the adjusted analyses for Models 4 through 6 (Table 13-59(h): $p=0.012$, Adj. Slope=0.0090; $p=0.001$, Adj. Slope=0.0102; and $p=0.040$, Adj. Slope=0.0066 for Models 4, 5, and 6 respectively). All of the adjusted analyses contained three covariate-by-covariate interactions: race-by-current alcohol use, occupation-by-degreasing chemical exposure, and lifetime alcohol history-by-degreasing chemical exposure.

Transferrin (Discrete)

The unadjusted Model 1 analysis did not reveal a significant group difference in the percentage of individuals with low transferrin levels (Table 13-60(a): $p>0.11$ for all contrasts). The interaction between group and lifetime alcohol history was significant in the adjusted Model 1 analysis (Table 13-60(a): $p=0.007$). Appendix Table I-2-44 displays adjusted results stratified by lifetime alcohol history. In addition to the group-by-lifetime alcohol history interaction, the final model also included race, current alcohol use, and two covariate-by-covariate interactions: age-by-degreasing chemical exposure and degreasing

Table 13-60.
Analysis of Transferrin
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Low**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***939***	***11.9***	***0.82 (0.64,1.06)***	***0.149***
	Comparison	***1,253***	***14.1***		
Officer	Ranch Hand	361	12.2	0.78 (0.52,1.16)	0.255
	Comparison	495	15.2		
Enlisted Flyer	Ranch Hand	162	16.7	1.25 (0.70,2.23)	0.540
	Comparison	196	13.8		
Enlisted Groundcrew	Ranch Hand	416	9.9	0.71 (0.47,1.06)	0.117
	Comparison	562	13.3		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***0.81 (0.63,1.06)*****	***0.120*****	GROUP*DRKYR (p=0.007) RACE (p=0.003) ALC (p=0.001) AGE*DC (p=0.010) DC*DRKYR (p=0.004)
Officer	0.74 (0.49,1.11)**	0.144**	
Enlisted Flyer	1.21 (0.67,2.20)**	0.524**	
Enlisted Groundcrew	0.74 (0.49,1.12)**	0.153**	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

** Group-by-covariate interaction ($p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-44 for further analysis of this interaction.

Table 13-60. (Continued)
Analysis of Transferrin
(Discrete)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Low	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	173	10.4	0.91 (0.72,1.14)	0.403
Medium	170	10.6		
High	172	8.1		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
508	0.94 (0.72,1.22)	0.630	OCC*DC (p=0.021) OCC*ALC (p=0.025)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 13-60. (Continued)
Analysis of Transferrin
(Discrete)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	**n**	**Percent Low**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,043	14.7		
Background RH	369	14.1	0.97 (0.69,1.37)	0.863
Low RH	257	10.5	0.67 (0.43,1.03)	0.071
High RH	258	8.9	0.56 (0.36,0.90)	0.015
Low plus High RH	515	9.7	0.62 (0.44,0.87)	0.005

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	**n**	**Adj. Relative Risk (95% C.I.)[ac]**	**p-Value**	**Covariate Remarks**
Comparison	1,025			DXCAT*DRKYR (p=0.033) RACE (p=0.024) ALC (p<0.001) DC*AGE (p=0.008) DC*DRKYR (p=0.010)
Background RH	362	0.94 (0.66,1.34)**	0.730**	
Low RH	251	0.64 (0.41,1.00)**	0.052**	
High RH	251	0.61 (0.38,0.98)**	0.042**	
Low plus High RH	502	0.63 (0.44,0.89)**	0.009**	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interaction ($0.01<p\leq0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction; refer to Appendix Table I-2-44 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 13-60. (Continued)
Analysis of Transferrin
(Discrete)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Low/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	12.4 (290)	12.4 (298)	9.8 (296)	0.86 (0.75,1.00)	0.049
5	12.9 (294)	12.1 (297)	9.6 (293)	0.89 (0.79,1.00)	0.053
6[c]	13.0 (293)	12.1 (297)	9.6 (293)	0.88 (0.77,1.00)	0.048

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	864	0.84 (0.71,0.99)	0.043	OCC*DC (p=0.031) IC*DRKYR (p=0.020) AGE*DC (p=0.019) DC*DRKYR (p<0.001)
5	864	0.86 (0.75,0.99)	0.041	OCC*DC (p=0.030) IC*DRKYR (p=0.019) AGE*DC (p=0.020) DC*DRKYR (p<0.001)
6[d]	863	0.85 (0.73,0.99)	0.039	OCC*DC (p=0.032) IC*DRKYR (p=0.019) AGE*DC (p=0.020) DC*DRKYR (p<0.001)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

chemical exposure-by-lifetime alcohol history. The adjusted Model 1 analysis did not reveal a significant group contrast when the group-by-lifetime alcohol history interaction was removed from the final model (Table 13-60(b): $p \geq 0.12$ for all contrasts).

The unadjusted Model 2 results did not show a significant association between transferrin and initial dioxin (Table 13-60(c,d): $p > 0.40$ for both analyses). The adjusted Model 2 analysis contained two covariate-by-covariate interactions: occupation-by-degreasing chemical exposure and occupation-by-current alcohol use.

The unadjusted Model 3 analysis showed that the high Ranch hands and low plus high Ranch Hands had significantly fewer low abnormalities than the Comparisons (Table 13-60(e): p=0.015, Est. RR=0.56, 95% C.I.=[0.36, 0.90]; p=0.005, Est. RR=0.62, 95% C.I.=[0.44, 0.87]) and that the low Ranch Hands had marginally fewer abnormalities than the Comparisons (Table 13-60(f): p=0.071, Est. RR=0.67, 95% C.I.=[0.43, 1.03]).

Categorized dioxin-by-lifetime alcohol history was a significant interaction in the adjusted analysis of Model 3 (Table 13-60(f): p=0.033). Appendix Table I-2-44 presents adjusted results stratified by lifetime alcohol history. The final model also included race, current alcohol use, and two covariate-by-covariate interactions: degreasing chemical exposure-by-age and degreasing chemical exposure-by-lifetime alcohol history. When the categorized dioxin-by-lifetime alcohol history interaction was removed from the final model, the adjusted Model 3 results paralleled the unadjusted results. The adjusted analysis revealed significant contrasts for the high Ranch Hands and the low plus high Ranch Hands (Table 13-60(f): p=0.042, Adj. RR=0.61, 95% C.I.=[0.38, 0.98]; p=0.009, Adj. RR=0.63, 95% C.I.=[0.44, 0.89]).

The mean levels of transferrin from the continuous analysis were generally higher for the Ranch Hands than for the Comparisons, while the relative risks from the Model 3 discrete analysis of transferrin were less than 1.00. These results are consistent because low levels of transferrin are considered abnormal.

The unadjusted analyses for Models 4 and 6 detected a significant inverse association between transferrin and current dioxin (Table 13-60(g): p=0.049, Est. RR=0.86, 95% C.I.=[0.75, 1.00] and p=0.048, Adj. RR=0.88, 95% C.I.=[0.77, 1.00]). For Model 5, the unadjusted analysis revealed a marginally significant inverse association between transferrin and current dioxin (Table 13-60(g): p=0.053, Est. RR=0.89, 95% C.I.=[0.79, 1.00]).

Each of the adjusted analyses for Models 4 through 6 revealed a significant inverse association between transferrin and current dioxin (Table 13-60(h): p=0.043, Adj. RR=0.84, 95% C.I.=[0.71, 0.99]; p=0.041, Adj. RR=0.86, 95% C.I.=[0.75, 0.99]; and p=0.039, Adj. RR=0.85, 95% C.I.=[0.73, 0.99] for Models 4, 5, and 6 respectively). All of the adjusted analyses contained four covariate-by-covariate interactions: occupation-by-degreasing chemical exposure, industrial chemical exposure-by-lifetime alcohol history, age-by-degreasing chemical exposure, and degreasing chemical exposure-by-lifetime alcohol history.

Removing occupation from the analyses of Models 4 through 6 caused the association between transferrin and current dioxin to become nonsignificant in Models 4 and 5 (Appendix Table I-3-47(b): $p > 0.10$ for both analyses) and to become marginally significant in Model 6 (Appendix Table I-3-47(b): $p = 0.098$, Adj. RR=0.89, 95% C.I.=[0.77, 1.02]).

The analyses of Models 4 through 6 for transferrin in its continuous form found a significant positive association with current dioxin. By contrast, the analyses of Models 4 through 6 for transferrin in its discrete form with occupation uncovered a significant inverse association with current dioxin. The results are consistent because low levels of transferrin are considered abnormal.

Longitudinal Analysis

Longitudinal analyses were conducted on seven variables (AST, ALT, GGT, cholesterol, HDL cholesterol, cholesterol-HDL ratio, and triglycerides) in both their discrete and continuous forms to examine whether changes over time differed with respect to group membership (Model 1), initial dioxin (Model 2), and categorized dioxin (Model 3). Models 4, 5, and 6 were not examined in the longitudinal analyses because current dioxin is the measure of exposure in these models, changes over time, and is not available for all participants for 1982, 1985, or 1992. For all seven variables, the longitudinal analyses investigated the differences between the 1982 examination and the 1992 examination. The measurement procedure used in 1992 (Paramax®) differed from the measurement procedure used in the previous three examinations (ACA). The effect of this change in methods was minimal and is discussed further in Chapter 7, Statistical Methods.

The continuous longitudinal analyses examined the paired differences between the measurements from 1982 and 1992. These paired differences measured the change in the seven variables over time. Each of the three models used in the longitudinal analysis adjusted for age and the 1982 measurement of the variable being analyzed. The analyses of Models 2 and 3 also were adjusted for percent body fat at the time of duty in SEA and the change in the percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

The discrete longitudinal analyses examined relative risks at the 1992 examination for participants who were classified as normal at the 1982 examination. Participants considered abnormal in 1982 were excluded because the focus of the analyses was on investigating the temporal effects of dioxin during the period between 1982 and 1992. Participants considered abnormal in 1982 were already abnormal before this period; consequently, only participants considered normal at the 1982 examination were considered to be at risk when the effects of dioxin over time were explored. The rate of abnormalities under this restriction approximates an incidence rate between 1982 and 1992. All three models were adjusted for age; Models 2 and 3 also were adjusted for percent body fat at the time of duty in SEA and the change in the percent body fat from the time of duty in SEA to the data of the blood draw for dioxin.

Laboratory Examination Variables

AST (Continuous)

In the Model 1 analysis, examination of the paired differences between 1982 and 1992 for AST did not reveal a significant group difference (Table 13-61(a): $p>0.12$ for all contrasts). The Model 2 analysis did not show a significant association between the paired differences and initial dioxin (Table 13-61(b): $p=0.486$). For Model 3, the longitudinal analysis did not show any of the Ranch Hand categories to be significantly different from the Comparison group (Table 13-61(c): $p>0.13$ for all contrasts).

AST (Discrete)

The analysis for Model 1 did not reveal a significant group difference in the percentage of individuals with high AST levels for participants who had normal AST levels in 1982 (Table 13-62(a): $p>0.45$ for all contrasts). Examination of the Model 2 longitudinal results did not reveal a significant association between initial dioxin and the percentage of individuals having high AST levels (Table 13-62(b): $p=0.637$). Similarly, the Model 3 analysis did not detect a significant difference between any of the Ranch Hand categories and the Comparison group (Table 13-62(c): $p>0.20$ for all contrasts).

In both the Ranch Hand and Comparison cohorts, the percentage of participants with high AST levels showed a marked decrease between 1982 and 1992. This decrease between 1982 and 1992 may partially be attributed to the change in definition of an abnormal high AST level between the 1982 and 1992 examinations. AST abnormalities for the 1982, 1985, 1987, and 1992 examinations were defined as greater than 41 U/L, 47 U/L, 47 U/L, and 50 U/L respectively. Regardless of how the definition of abnormality varied over time, the change in AST over time was similar in both Ranch Hands and Comparisons in Models 1 and 3 and was not associated with dioxin levels in Model 2.

ALT (Continuous)

The longitudinal analysis of Model 1 did not show a significant group difference in the mean paired differences (Table 13-63(a): $p>0.12$ for all contrasts). The Model 2 results did not reveal a significant association between initial dioxin and the paired differences (Table 13-63(b): $p=0.995$). The Model 3 analysis did not show a significant difference between any of the Ranch Hand categories and the Comparison group (Table 13-63(c): $p>0.15$ for all contrasts).

ALT (Discrete)

The longitudinal analysis of Model 1 did not reveal a significant overall group difference in the percentage of individuals with high levels of ALT for participants who had normal ALT levels in 1982 (Table 13-64(a): $p=0.299$). However, the stratified occupation analysis detected a marginally significant adjusted relative risk less than 1.00 for the enlisted groundcrew ($p=0.052$, Adj. RR=0.53, 95% C.I.=[0.28, 1.00]). Of the enlisted

Table 13-61.
Longitudinal Analysis of AST (U/L)
(Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS								
		Mean[a]/(n) Examination						
Occupational Category	Group	1982	1985	1987	1992	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
All	***Ranch Hand***	***32.47 (884)***	***33.36 (862)***	***25.47 (855)***	***23.09 (884)***	***-9.38***	***-0.27***	***0.231***
	Comparison	***32.76 (1,038)***	***33.49 (1,014)***	***25.49 (1,008)***	***23.66 (1,038)***	***-9.10***		
Officer	Ranch Hand	32.49 (332)	34.00 (326)	25.99 (327)	23.72 (332)	-8.76	0.19	0.661
	Comparison	33.29 (398)	33.63 (390)	25.98 (384)	24.33 (398)	-8.96		
Enlisted Flyer	Ranch Hand	31.81 (158)	32.33 (156)	24.32 (153)	21.31 (158)	-10.49	-0.80	0.122
	Comparison	32.66 (169)	33.54 (166)	24.90 (167)	22.96 (169)	-9.69		
Enlisted Groundcrew	Ranch Hand	32.73 (394)	33.23 (380)	25.50 (375)	23.31 (394)	-9.41	-0.40	0.723
	Comparison	32.37 (471)	33.35 (458)	25.29 (457)	23.36 (471)	-9.01		

[a] Transformed from natural logarithm scale.

[b] Difference between 1992 and 1982 examination means after transformation to original scale.

[c] P-value is based on analysis of natural logarithm of AST; results adjusted for natural logarithm of AST in 1982 and age in 1992.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations.

Table 13-61. (Continued)
Longitudinal Analysis of AST (U/L)
(Continuous)

b) MODEL 2: RANCH HANDS — INITIAL DIOXIN						
Initial Dioxin Category Summary Statistics					Analysis Results for Log_2 (Initial Dioxin)[b]	
	Mean[a]/(n) Examination					
Initial Dioxin	1982	1985	1987	1992	Adj. Slope (Std. Error)	p-Value
Low	33.18 (166)	34.29 (162)	25.34 (165)	22.48 (166)	0.009 (0.013)	0.486
Medium	33.43 (166)	34.00 (161)	25.92 (162)	23.39 (166)		
High	33.37 (166)	33.33 (163)	26.12 (160)	23.76 (166)		

[a] Transformed from natural logarithm scale.

[b] Results based on difference between natural logarithm of AST in 1992 and natural logarithm of AST in 1982 versus $\log_2$ (initial dioxin); results adjusted for percent body fat at the time of duty in SEA, the change in percent body fat from the time of duty in SEA to the date of blood draw for dioxin, natural logarithm of 1982 AST, and age in 1992.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations.

Table 13-61. (Continued)
Longitudinal Analysis of AST (U/L)
(Continuous)

c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY							
	Mean[a]/(n) Examination						
Dioxin Category	1982	1985	1987	1992	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
Comparison	32.73 (896)	33.45 (884)	25.54 (883)	23.59 (896)	-9.13		
Background RH	31.39 (335)	32.61 (332)	25.06 (330)	22.87 (335)	-8.52	0.61	0.899
Low RH	33.09 (247)	34.42 (241)	25.67 (245)	23.25 (247)	-9.84	-0.71	0.384
High RH	33.56 (251)	33.34 (245)	25.90 (242)	23.16 (251)	-10.40	-1.27	0.140
Low plus High RH	33.33 (498)	33.87 (486)	25.79 (487)	23.21 (498)	-10.12	-0.99	0.132

[a] Transformed from natural logarithm scale.

[b] Difference between 1992 and 1982 examination means after transformation to original scale.

[c] P-value is based on analysis of natural logarithm of AST; results adjusted for percent body fat at the time of duty in SEA, the change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, natural logarithm of AST in 1982, and age in 1992.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤10 ppt.
Background (Ranch Hand): Current Dioxin ≤10 ppt.
Low (Ranch Hand): Current Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤143 ppt.
High (Ranch Hand): Current Dioxin >10 ppt, Initial Dioxin >143 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations.

Table 13-62.
Longitudinal Analysis of AST
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS					
		Percent High/(n) Examination			
Occupational Category	Group	1982	1985	1987	1992
All	*Ranch Hand*	*11.8 (884)*	*6.5 (862)*	*4.0 (855)*	*2.8 (884)*
	Comparison	*13.1 (1,038)*	*7.4 (1,014)*	*3.5 (1,008)*	*3.7 (1,038)*
Officer	Ranch Hand	10.5 (332)	8.0 (326)	4.9 (327)	3.9 (332)
	Comparison	14.6 (398)	6.4 (390)	4.4 (384)	4.3 (398)
Enlisted Flyer	Ranch Hand	11.4 (158)	5.1 (156)	2.6 (153)	1.3 (158)
	Comparison	13.0 (169)	8.4 (166)	3.6 (167)	3.6 (169)
Enlisted Groundcrew	Ranch Hand	12.9 (394)	5.8 (380)	3.7 (375)	2.5 (394)
	Comparison	11.9 (471)	7.9 (458)	2.6 (457)	3.2 (471)

		Normal in 1982			
Occupational Category	Group	n in 1992	Percent High in 1992	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	*Ranch Hand*	*780*	*1.8*	*0.73 (0.37,1.44)*	*0.360*
	Comparison	*902*	*2.4*		
Officer	Ranch Hand	297	1.7	0.63 (0.21,1.89)	0.408
	Comparison	340	2.7		
Enlisted Flyer	Ranch Hand	140	1.4	0.70 (0.11,4.25)	0.696
	Comparison	147	2.0		
Enlisted Groundcrew	Ranch Hand	343	2.0	0.85 (0.32,2.26)	0.744
	Comparison	415	2.4		

[a] Relative risk, confidence interval, and p-values are in reference to a contrast of 1982 and 1992 results; results adjusted for age in 1992.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations. Statistical analyses are based only on participants who had a normal AST level in 1982 (see Chapter 7, Statistical Methods).

Table 13-62. (Continued)
Longitudinal Analysis of AST
(Discrete)

b) MODEL 2: RANCH HANDS — INITIAL DIOXIN				
	Percent High/(n) Examination			
Initial Dioxin	1982	1985	1987	1992
Low	12.1 (166)	7.4 (162)	4.2 (165)	2.4 (166)
Medium	19.3 (166)	6.2 (161)	2.5 (162)	3.0 (166)
High	13.9 (166)	8.6 (163)	5.0 (160)	3.0 (166)

Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)[a]	
	Normal in 1982			
Initial Dioxin	n in 1992	Percent High in 1992	Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	146	1.4	1.13 (0.68,1.90)	0.637
Medium	134	2.2		
High	143	2.1		

[a] Adjusted for percent body fat at the time of duty in SEA, the change in percent body fat from the time of duty in SEA to the date of blood draw for dioxin, and age in 1992.

[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations. Statistical analyses are based only on participants who had a normal AST level in 1982 (see Chapter 7, Statistical Methods).

Table 13-62. (Continued)
Longitudinal Analysis of AST
(Discrete)

c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY				
	Percent High/(n) Examination			
Dioxin Category	**1982**	**1985**	**1987**	**1992**
Comparison	13.0 (896)	7.0 (884)	3.4 (883)	3.2 (896)
Background RH	6.9 (335)	5.1 (332)	4.2 (330)	2.4 (335)
Low RH	12.6 (247)	7.5 (241)	4.1 (245)	3.6 (247)
High RH	17.5 (251)	7.4 (245)	3.7 (242)	2.0 (251)
Low plus High RH	15.1 (498)	7.4 (486)	3.9 (487)	2.8 (498)

	Normal in 1982			
Dioxin Category	**n in 1992**	**Percent High in 1992**	**Adj. Relative Risk (95% C.I.)[ab]**	**p-Value[b]**
Comparison	780	2.3		
Background RH	312	1.0	0.45 (0.13,1.55)	0.203
Low RH	216	2.3	0.98 (0.36,2.70)	0.975
High RH	207	1.5	0.61 (0.18,2.12)	0.438
Low plus High RH	423	1.9	0.80 (0.34,1.87)	0.609

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA, the change in percent body fat from the time of duty in SEA to the date of blood draw for dioxin, and age in 1992.

Note: RH = Ranch Hand.
Comparison: Current Dioxin $\leq$10 ppt.
Background (Ranch Hand): Current Dioxin $\leq$10 ppt.
Low (Ranch Hand): Current Dioxin $>$10 ppt, 10 ppt $<$ Initial Dioxin $\leq$143 ppt.
High (Ranch Hand): Current Dioxin $>$10 ppt, Initial Dioxin $>$ 143 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations. Statistical analyses are based only on participants who had a normal AST level in 1982 (see Chapter 7, Statistical Methods).

Table 13-63.
Longitudinal Analysis of ALT (U/L)
(Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS								
		Mean[a]/(n) Examination						
Occupational Category	Group	1982	1985	1987	1992	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
All	***Ranch Hand***	***19.85 (884)***	***21.58 (862)***	***20.51 (855)***	***26.90 (884)***	***7.05***	***-0.31***	***0.263***
	Comparison	***20.37 (1,038)***	***22.43 (1,014)***	***20.59 (1,008)***	***27.74 (1,038)***	***7.37***		
Officer	Ranch Hand	19.72 (332)	22.10 (326)	20.81 (327)	26.86 (332)	7.13	0.24	0.996
	Comparison	20.40 (398)	22.02 (390)	20.42 (384)	27.30 (398)	6.89		
Enlisted Flyer	Ranch Hand	18.80 (158)	20.76 (156)	19.69 (153)	24.87 (158)	6.07	-0.94	0.128
	Comparison	20.57 (169)	22.15 (166)	20.21 (167)	27.59 (169)	7.02		
Enlisted Groundcrew	Ranch Hand	20.38 (394)	21.48 (380)	20.60 (375)	27.79 (394)	7.41	-0.49	0.482
	Comparison	20.27 (471)	22.89 (458)	20.88 (457)	28.17 (471)	7.90		

[a] Transformed from natural logarithm scale.

[b] Difference between 1992 and 1982 examination means after transformation to original scale.

[c] P-value is based on analysis of natural logarithm of ALT; results adjusted for natural logarithm of ALT in 1982 and age in 1992.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations.

Table 13-63. (Continued)
Longitudinal Analysis of ALT (U/L)
(Continuous)

b) MODEL 2: RANCH HANDS — INITIAL DIOXIN						
Initial Dioxin Category Summary Statistics					Analysis Results for Log_2 (Initial Dioxin)[b]	
	Mean[a]/(n) Examination					
Initial Dioxin	1982	1985	1987	1992	Adj. Slope (Std. Error)	p-Value
Low	20.76 (166)	22.12 (162)	19.68 (165)	26.16 (166)	0.00001 (0.015)	0.995
Medium	21.89 (166)	23.57 (161)	22.00 (162)	28.45 (166)		
High	22.84 (166)	23.65 (163)	23.35 (160)	29.50 (166)		

[a] Transformed from natural logarithm scale.

[b] Results based on difference between natural logarithm of ALT in 1992 and natural logarithm of ALT in 1982 versus $\log_2$ (initial dioxin); results adjusted for percent body fat at the time of duty in SEA, the change in percent body fat from the time of duty in SEA to the date of blood draw for dioxin, natural logarithm of 1982 ALT, and age in 1992.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations.

Table 13-63. (Continued)
Longitudinal Analysis of ALT (U/L)
(Continuous)

c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY							
	Mean[a]/(n) Examination						
Dioxin Category	1982	1985	1987	1992	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
Comparison	20.43 (896)	22.58 (884)	20.73 (883)	27.64 (896)	7.22		
Background RH	17.34 (335)	19.64 (332)	19.09 (330)	25.24 (335)	7.91	0.69	0.773
Low RH	20.90 (247)	22.94 (241)	20.49 (245)	27.47 (247)	6.56	-0.65	0.890
High RH	22.75 (251)	23.27 (245)	22.79 (242)	28.54 (251)	5.79	-1.43	0.152
Low plus High RH	21.82 (498)	23.10 (486)	21.60 (487)	28.00 (498)	6.19	-1.03	0.314

[a] Transformed from natural logarithm scale.

[b] Difference between 1992 and 1982 examination means after transformation to original scale.

[c] P-value is based on analysis of natural logarithm of ALT; results adjusted for percent body fat at the time of duty in SEA, the change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, natural logarithm of ALT in 1982, and age in 1992.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤10 ppt.
Background (Ranch Hand): Current Dioxin ≤10 ppt.
Low (Ranch Hand): Current Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤143 ppt.
High (Ranch Hand): Current Dioxin >10 ppt, Initial Dioxin >143 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations.

Table 13-64.
Longitudinal Analysis of ALT
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS					
		Percent High/(n) Examination			
Occupational Category	Group	1982	1985	1987	1992
All	*Ranch Hand*	*7.0 (884)*	*13.7 (862)*	*11.9 (855)*	*5.7 (884)*
	Comparison	*7.4 (1,038)*	*14.4 (1,014)*	*10.7 (1,008)*	*6.8 (1,038)*
Officer	Ranch Hand	6.6 (332)	16.6 (326)	13.1 (327)	6.3 (332)
	Comparison	7.0 (398)	12.8 (390)	11.2 (384)	5.3 (398)
Enlisted Flyer	Ranch Hand	7.0 (158)	10.3 (156)	9.2 (153)	4.4 (158)
	Comparison	8.9 (169)	13.9 (166)	8.4 (167)	6.5 (169)
Enlisted Groundcrew	Ranch Hand	7.4 (394)	12.6 (380)	12.0 (375)	5.6 (394)
	Comparison	7.2 (471)	15.9 (458)	11.2 (457)	8.3 (471)

		Normal in 1982			
Occupational Category	Group	n in 1992	Percent High in 1992	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	*Ranch Hand*	*822*	*4.3*	*0.79 (0.51,1.23)*	*0.299*
	Comparison	*961*	*5.3*		
Officer	Ranch Hand	310	5.2	1.41 (0.68,2.94)	0.359
	Comparison	370	3.8		
Enlisted Flyer	Ranch Hand	147	2.7	0.82 (0.22,3.13)	0.774
	Comparison	154	3.3		
Enlisted Groundcrew	Ranch Hand	365	4.1	0.53 (0.28,1.00)	0.052
	Comparison	437	7.3		

[a] Relative risk, confidence interval, and p-values are in reference to a contrast of 1982 and 1992 results; results adjusted for age in 1992.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations. Statistical analyses are based only on participants who had a normal ALT level in 1982 (see Chapter 7, Statistical Methods).

Table 13-64. (Continued)
Longitudinal Analysis of ALT
(Discrete)

b) MODEL 2: RANCH HANDS — INITIAL DIOXIN				
	Percent High/(n) Examination			
Initial Dioxin	1982	1985	1987	1992
Low	7.8 (166)	13.6 (162)	7.3 (165)	2.4 (166)
Medium	7.2 (166)	14.9 (161)	14.2 (162)	8.4 (166)
High	12.1 (166)	17.2 (163)	16.3 (160)	7.8 (166)

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
	Normal in 1982			
Initial Dioxin	n in 1992	Percent High in 1992	Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	153	2.6	0.94 (0.65,1.36)	0.739
Medium	154	6.5		
High	146	3.4		

[a] Adjusted for percent body fat at the time of duty in SEA, the change in percent body fat from the time of duty in SEA to the date of blood draw for dioxin, and age in 1992.

[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations. Statistical analyses are based only on participants who had a normal ALT level in 1982 (see Chapter 7, Statistical Methods).

Table 13-64. (Continued)
Longitudinal Analysis of ALT
(Discrete)

c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY				
	Percent High/(n) Examination			
Dioxin Category	1982	1985	1987	1992
Comparison	7.5 (896)	14.6 (884)	11.2 (883)	6.8 (896)
Background RH	4.2 (335)	11.5 (332)	10.9 (330)	4.2 (335)
Low RH	7.3 (247)	14.1 (241)	10.2 (245)	5.3 (247)
High RH	10.8 (251)	16.3 (245)	14.9 (242)	7.2 (251)
Low plus High RH	9.0 (498)	15.2 (486)	12.5 (487)	6.2 (498)

	Normal in 1982			
Dioxin Category	n in 1992	Percent High in 1992	Adj. Relative Risk (95% C.I.)[ab]	p-Value[b]
Comparison	829	5.3		
Background RH	321	3.4	0.79 (0.40,1.56)	0.494
Low RH	229	4.4	0.87 (0.43,1.77)	0.699
High RH	224	4.0	0.60 (0.28,1.25)	0.172
Low plus High RH	453	4.2	0.72 (0.41,1.25)	0.239

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA, the change in percent body fat from the time of duty in SEA to the date of blood draw for dioxin, and age in 1992.

Note: RH = Ranch Hand.
Comparison: Current Dioxin $\leq$10 ppt.
Background (Ranch Hand): Current Dioxin $\leq$10 ppt.
Low (Ranch Hand): Current Dioxin >10 ppt, 10 ppt < Initial Dioxin $\leq$143 ppt.
High (Ranch Hand): Current Dioxin >10 ppt, Initial Dioxin > 143 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations. Statistical analyses are based only on participants who had a normal ALT level in 1982 (see Chapter 7, Statistical Methods).

groundcrew who did not have high ALT levels in 1982, Ranch Hands were less likely than Comparisons to have high levels of ALT at the 1992 examination (4.1% vs. 7.3%).

Examination of the Model 2 results did not show a significant association between initial dioxin and the percentage of participants having high ALT levels (Table 13-64(b): $p=0.739$). The longitudinal analysis of Model 3 did not reveal any of the Ranch Hand categories to be significantly different from the Comparison group (Table 13-64(c): $p>0.17$ for all contrasts).

In both the Ranch Hand and Comparison cohorts, the percentage of participants with high ALT levels showed a marked increase between 1982 and 1985 and a marked decrease between 1987 and 1992. These changes may be partly attributable to the change in abnormal cutpoints across examinations. The abnormal cutpoints for ALT were 45 U/L, 36 U/L, 36 U/L, and 55 U/L for the 1982, 1985, 1987, and 1992 laboratory examinations respectively. Thus the increase in abnormalities seen between 1982 and 1985 may be partially explained by the lower cutpoint in 1985, while the decrease between 1987 and 1992 may be partly due to the higher cutpoint in 1992. Differences between the 1992 results and other examinations may also be partly due to the change in measurement procedure between examinations (ACA in 1982, 1985 and 1987 vs. Paramax® in 1992).

GGT (Continuous)

Examination of the mean paired differences for GGT in Model 1 did not show the Ranch Hands to differ significantly from the Comparisons (Table 13-65(a): $p>0.14$ for all contrasts). The longitudinal analysis of Model 2 did not show a significant association between initial dioxin and the paired differences (Table 13-65(b): $p=0.944$). For Model 3, the longitudinal analysis did not detect a significant difference between any of the Ranch Hand categories and the Comparison group (Table 13-65(c): $p>0.20$ for all contrasts).

GGT (Discrete)

The longitudinal analysis of Model 1 did not reveal a significant group difference in the percentage of individuals with high GGT levels for participants who had normal GGT levels in 1982 (Table 13-66(a): $p>0.12$ for all contrasts). The results from the Model 2 longitudinal analysis did not reveal a significant association between initial dioxin and GGT (Table 13-66(b): $p=0.628$). For Model 3, the longitudinal analysis did not show any of the Ranch Hand categories to be significantly different from the Comparison group (Table 13-66(c): $p>0.31$ for all contrasts).

In both the Ranch Hand and Comparison cohorts, the percentage of participants having high GGT levels showed a noticeable increase between 1987 and 1992. This may partially be attributed to the change in the definition of a high GGT level between the 1987 and 1992 examinations and the change in the measurement procedure between the two examinations (ACA in 1987 versus Paramax in 1992). In 1987, a high GGT level was defined as at least 86 U/L, whereas in 1992, a high GGT level was defined as greater than 51 U/L.

Table 13-65.
Longitudinal Analysis of GGT (U/L)
(Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS								
		Mean[a]/(n) Examination						
Occupational Category	Group	1982	1985	1987	1992	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
All	*Ranch Hand*	*38.21 (884)*	*31.71 (862)*	*32.27 (855)*	*32.98 (884)*	*-5.23*	*0.92*	*0.200*
	Comparison	*38.26 (1,038)*	*31.86 (1,014)*	*32.00 (1,008)*	*32.11 (1,038)*	*-6.15*		
Officer	Ranch Hand	36.91 (332)	31.48 (326)	32.36 (327)	32.51 (332)	-4.40	0.96	0.373
	Comparison	36.97 (398)	30.86 (390)	31.35 (384)	31.61 (398)	-5.36		
Enlisted Flyer	Ranch Hand	38.58 (158)	31.58 (156)	31.55 (153)	31.40 (158)	-7.18	0.45	0.580
	Comparison	42.06 (169)	34.43 (166)	33.56 (167)	34.43 (169)	-7.63		
Enlisted Groundcrew	Ranch Hand	39.19 (394)	31.96 (380)	32.49 (375)	34.04 (394)	-5.15	1.19	0.146
	Comparison	38.07 (471)	31.82 (458)	32.00 (457)	31.73 (471)	-6.34		

[a] Transformed from natural logarithm scale.

[b] Difference between 1992 and 1982 examination means after transformation to original scale.

[c] P-value is based on analysis of natural logarithm of GGT; results adjusted for natural logarithm of GGT in 1982 and age in 1992.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations.

Table 13-65. (Continued)
Longitudinal Analysis of GGT (U/L)
(Continuous)

b) MODEL 2: RANCH HANDS — INITIAL DIOXIN						
	Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]	
	Mean[a]/(n) Examination					
Initial Dioxin	1982	1985	1987	1992	Adj. Slope (Std. Error)	p-Value
Low	41.86 (166)	34.28 (162)	32.38 (165)	33.12 (166)	-0.001 (0.018)	0.944
Medium	42.44 (166)	35.59 (161)	36.37 (162)	36.72 (166)		
High	42.30 (166)	33.95 (163)	35.76 (160)	36.54 (166)		

[a] Transformed from natural logarithm scale.

[b] Results based on difference between natural logarithm of GGT in 1992 and natural logarithm of GGT in 1982 versus $\log_2$ (initial dioxin); results adjusted for percent body fat at the time of duty in SEA, the change in percent body fat from the time of duty in SEA to the date of blood draw for dioxin, natural logarithm of 1982 GGT, and age in 1992.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations.

Table 13-65. (Continued)
Longitudinal Analysis of GGT (U/L)
(Continuous)

c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY							
	Mean[a]/(n) Examination						
Dioxin Category	1982	1985	1987	1992	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
Comparison	37.91 (896)	31.68 (884)	31.89 (883)	31.70 (896)	-6.21		
Background RH	33.01 (335)	27.85 (332)	28.87 (330)	29.35 (335)	-3.66	2.55	0.207
Low RH	41.69 (247)	34.50 (241)	33.47 (245)	34.81 (247)	-6.88	-0.67	0.346
High RH	42.70 (251)	34.69 (245)	36.15 (242)	36.03 (251)	-6.67	-0.46	0.536
Low plus High RH	42.20 (498)	34.60 (486)	34.77 (487)	35.42 (498)	-6.78	-0.56	0.315

[a] Transformed from natural logarithm scale.

[b] Difference between 1992 and 1982 examination means after transformation to original scale.

[c] P-value is based on analysis of natural logarithm of GGT; results adjusted for percent body fat at the time of duty in SEA, the change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, natural logarithm of GGT in 1982, and age in 1992.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤10 ppt.
Background (Ranch Hand): Current Dioxin ≤10 ppt.
Low (Ranch Hand): Current Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤143 ppt.
High (Ranch Hand): Current Dioxin >10 ppt, Initial Dioxin >143 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations.

Table 13-66.
Longitudinal Analysis of GGT
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS

Occupational Category	Group	Percent High/(n) Examination 1982	1985	1987	1992
All	*Ranch Hand*	*8.6 (884)*	*7.5 (862)*	*7.4 (855)*	*20.5 (884)*
	Comparison	*9.3 (1,038)*	*8.3 (1,014)*	*7.2 (1,008)*	*18.7 (1,038)*
Officer	Ranch Hand	9.0 (332)	7.4 (326)	8.6 (327)	19.9 (332)
	Comparison	9.1 (398)	8.0 (390)	7.3 (384)	18.3 (398)
Enlisted Flyer	Ranch Hand	10.1 (158)	7.7 (156)	7.8 (153)	18.4 (158)
	Comparison	11.8 (169)	10.8 (166)	10.2 (167)	20.7 (169)
Enlisted Groundcrew	Ranch Hand	7.6 (394)	7.6 (380)	6.1 (375)	21.8 (394)
	Comparison	8.5 (471)	7.6 (458)	6.1 (457)	18.3 (471)

Occupational Category	Group	Normal in 1982: n in 1992	Normal in 1982: Percent High in 1992	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	*Ranch Hand*	*808*	*15.8*	*1.23 (0.94,1.61)*	*0.127*
	Comparison	*942*	*13.3*		
Officer	Ranch Hand	302	15.6	1.34 (0.86,2.09)	0.195
	Comparison	362	12.2		
Enlisted Flyer	Ranch Hand	142	11.3	0.77 (0.39,1.55)	0.466
	Comparison	149	14.1		
Enlisted Groundcrew	Ranch Hand	364	17.9	1.34 (0.91,1.96)	0.135
	Comparison	431	13.9		

[a] Relative risk, confidence interval, and p-values are in reference to a contrast of 1982 and 1992 results; results adjusted for age in 1992.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations. Statistical analyses are based only on participants who had a normal GGT level in 1982 (see Chapter 7, Statistical Methods).

Table 13-66. (Continued)
Longitudinal Analysis of GGT
(Discrete)

b) MODEL 2: RANCH HANDS — INITIAL DIOXIN				
	Percent High/(n) Examination			
Initial Dioxin	1982	1985	1987	1992
Low	12.1 (166)	8.6 (162)	6.7 (165)	16.9 (166)
Medium	10.8 (166)	8.7 (161)	9.3 (162)	26.5 (166)
High	11.5 (166)	9.2 (163)	9.4 (160)	22.9 (166)

Initial Dioxin Category Summary Statistics			Analysis Results for Log₂ (Initial Dioxin)[a]	
	Normal in 1982			
Initial Dioxin	n in 1992	Percent High in 1992	Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	146	12.3	0.95 (0.77,1.17)	0.628
Medium	148	19.6		
High	147	15.7		

[a] Adjusted for percent body fat at the time of duty in SEA, the change in percent body fat from the time of duty in SEA to the date of blood draw for dioxin, and age in 1992.

[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations. Statistical analyses are based only on participants who had a normal GGT level in 1982 (see Chapter 7, Statistical Methods).

Table 13-66. (Continued)
Longitudinal Analysis of GGT
(Discrete)

c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY				
	Percent High/(n) Examination			
Dioxin Category	1982	1985	1987	1992
Comparison	8.8 (896)	8.5 (884)	6.9 (883)	18.1 (896)
Background RH	4.5 (335)	5.1 (332)	5.8 (330)	17.0 (335)
Low RH	11.7 (247)	8.3 (241)	7.4 (245)	21.1 (247)
High RH	11.2 (251)	9.4 (245)	9.5 (242)	23.1 (251)
Low plus High RH	11.5 (498)	8.9 (486)	8.4 (487)	22.1 (498)

	Normal in 1982			
Dioxin Category	n in 1992	Percent High in 1992	Adj. Relative Risk (95% C.I.)[ab]	p-Value[b]
Comparison	817	13.2		
Background RH	320	14.4	1.20 (0.82,1.75)	0.349
Low RH	218	15.6	1.23 (0.81,1.88)	0.328
High RH	223	16.1	1.14 (0.75,1.73)	0.535
Low plus High RH	441	15.9	1.19 (0.85,1.65)	0.311

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA, the change in percent body fat from the time of duty in SEA to the date of blood draw for dioxin, and age in 1992.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤10 ppt.
Background (Ranch Hand): Current Dioxin ≤10 ppt.
Low (Ranch Hand): Current Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤143 ppt.
High (Ranch Hand): Current Dioxin >10 ppt, Initial Dioxin > 143 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations. Statistical analyses are based only on participants who had a normal GGT level in 1982 (see Chapter 7, Statistical Methods).

Cholesterol (Continuous)

The longitudinal analysis of Model 1 revealed a marginally significant overall group difference for the mean paired differences (Table 13-67(a): p=0.074). The mean paired difference was greater for the Ranch Hands than the Comparisons (Table 13-67(a): 3.84 mg/dl vs. 0.47 mg/dl). For Model 2, the longitudinal analysis did not detect a significant association between initial dioxin and the paired differences for cholesterol (Table 13-67(b): p=0.052).

The longitudinal analysis for Model 3 revealed a marginally significant difference for the background Ranch Hands (Table 13-67(c): p=0.096). The mean paired differences were higher for the background Ranch Hands than for the Comparisons (Table 13-67(c): 5.53 mg/dl and -0.18 mg/dl respectively).

Cholesterol (Discrete)

For Model 1, the longitudinal analysis detected a significant overall group difference in the percentage of individuals with high cholesterol for participants who had normal cholesterol in 1982 (Table 13-68(a): p=0.037, Adj. RR=1.46, 95% C.I=[1.02, 2.10]). Of the participants with normal cholesterol levels in 1982, the Ranch Hands were more likely to have high cholesterol at the 1992 examination than the Comparisons (Table 13-68(a): 9.6% vs. 6.8%). In addition, the stratified occupation analysis revealed a marginally significant group difference in the enlisted flyer stratum (p=0.081, Adj. RR=2.20, 95% C.I.=[0.91, 5.34]). Of the enlisted flyers who had normal cholesterol in 1982, Ranch Hands were more than twice as likely as Comparisons to have high cholesterol at the 1992 examination (12.3% vs. 6.0%).

The longitudinal analysis for Model 2 did not show a significant association between initial dioxin and cholesterol (Table 13-68(b): p=0.717). Examination of the Model 3 results for the longitudinal analysis revealed a significant adjusted relative risk for the high Ranch Hands and a marginally significant relative risk for the low plus high Ranch Hands (Table 13-68(c): p=0.043, Adj. RR=1.76, 95% C.I.=[1.02, 3.03] and p=0.051, Adj. RR=1.55, 95% C.I.=[1.00, 2.40] respectively). Only 6.6 percent of the Comparisons with normal cholesterol in 1982 had high cholesterol at the 1992 examination, whereas 10.6 percent of the high Ranch Hands and 9.7 percent of the low plus high Ranch Hands with normal cholesterol in 1982 had high cholesterol at the 1992 examination.

HDL Cholesterol (Continuous)

Examination of the paired differences in the longitudinal analysis of Model 1 did not show a significant difference between the Ranch Hands and Comparisons (Table 13-69(a): p>0.61 for all contrasts). The longitudinal analysis for Model 2 did not reveal a significant association between initial dioxin and the paired differences for HDL cholesterol (Table 13-69(b): p=0.796). The Model 3 longitudinal analysis did not show a significant difference between any of the Ranch Hand categories and the Comparison group (Table 13-69(c): p>0.18).

Table 13-67.
Longitudinal Analysis of Cholesterol (mg/dl)
(Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS								
		Mean[a]/(n) Examination						
Occupational Category	Group	1982	1985	1987	1992	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
All	***Ranch Hand***	***211.16 (884)***	***214.00 (862)***	***214.08 (855)***	***215.00 (884)***	***3.84***	***3.37***	***0.074***
	Comparison	***213.93 (1,038)***	***215.61 (1,014)***	***214.22 (1,008)***	***214.40 (1,038)***	***0.47***		
Officer	Ranch Hand	211.99 (332)	214.78 (326)	214.14 (327)	213.51 (332)	1.52	3.06	0.177
	Comparison	212.72 (398)	214.64 (390)	213.14 (384)	211.18 (398)	-1.54		
Enlisted Flyer	Ranch Hand	215.26 (158)	218.43 (156)	216.04 (153)	218.50 (158)	3.24	5.14	0.458
	Comparison	222.73 (169)	220.90 (166)	220.73 (167)	220.83 (169)	-1.90		
Enlisted Groundcrew	Ranch Hand	208.85 (394)	211.55 (380)	213.23 (375)	214.86 (394)	6.01	3.02	0.352
	Comparison	211.88 (471)	214.54 (458)	212.79 (457)	214.87 (471)	2.99		

[a] Transformed from natural logarithm scale.

[b] Difference between 1992 and 1982 examination means after transformation to original scale.

[c] P-value is based on analysis of natural logarithm of cholesterol; results adjusted for natural logarithm of cholesterol in 1982 and age in 1992.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations.

Table 13-67. (Continued)
Longitudinal Analysis of Cholesterol (mg/dl)
(Continuous)

b) MODEL 2: RANCH HANDS — INITIAL DIOXIN						
Initial Dioxin Category Summary Statistics					Analysis Results for Log_2 (Initial Dioxin)[b]	
	Mean[a]/(n) Examination					
Initial Dioxin	1982	1985	1987	1992	Adj. Slope (Std. Error)	p-Value
Low	212.22 (166)	216.27 (162)	215.45 (165)	215.45 (166)	0.002 (0.005)	0.652
Medium	211.95 (166)	215.07 (161)	214.16 (162)	214.06 (166)		
High	214.85 (166)	216.38 (163)	217.67 (160)	218.11 (166)		

[a] Transformed from natural logarithm scale.

[b] Results based on difference between natural logarithm of cholesterol in 1992 and natural logarithm of cholesterol in 1982 versus log_2 (initial dioxin); results adjusted for percent body fat at the time of duty in SEA, the change in percent body fat from the time of duty in SEA to the date of blood draw for dioxin, natural logarithm of 1982 cholesterol, and age in 1992.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations.

Table 13-67. (Continued)
Longitudinal Analysis of Cholesterol (mg/dl)
(Continuous)

c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY							
	Mean[a]/(n) Examination						
Dioxin Category	1982	1985	1987	1992	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
Comparison	214.68 (896)	216.19 (884)	214.94 (883)	214.49 (896)	-0.18		
Background RH	207.62 (335)	210.99 (332)	211.88 (330)	213.21 (335)	5.59	5.78	0.096
Low RH	211.83 (247)	214.96 (241)	213.68 (245)	213.90 (247)	2.07	2.25	0.304
High RH	214.16 (251)	216.84 (245)	217.85 (242)	217.81 (251)	3.65	3.83	0.137
Low plus High RH	213.00 (498)	215.91 (486)	215.75 (487)	215.86 (498)	2.86	3.04	0.106

[a] Transformed from natural logarithm scale.

[b] Difference between 1992 and 1982 examination means after transformation to original scale.

[c] P-value is based on analysis of natural logarithm of cholesterol; results adjusted for percent body fat at the time of duty in SEA, the change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, natural logarithm of cholesterol in 1982, and age in 1992.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤10 ppt.
Background (Ranch Hand): Current Dioxin ≤10 ppt.
Low (Ranch Hand): Current Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤143 ppt.
High (Ranch Hand): Current Dioxin >10 ppt, Initial Dioxin >143 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations.

Table 13-68.
Longitudinal Analysis of Cholesterol
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS					
		Percent High/(n) Examination			
Occupational Category	Group	1982	1985	1987	1992
All	*Ranch Hand*	*14.9 (884)*	*15.9 (862)*	*16.3 (855)*	*14.7 (884)*
	Comparison	*15.8 (1,038)*	*18.4 (1,014)*	*14.2 (1,008)*	*12.8 (1,038)*
Officer	Ranch Hand	11.5 (332)	16.9 (326)	15.3 (327)	12.1 (332)
	Comparison	11.3 (398)	15.4 (390)	11.7 (384)	10.8 (398)
Enlisted Flyer	Ranch Hand	17.7 (158)	17.3 (156)	19.0 (153)	19.0 (158)
	Comparison	21.3 (169)	24.1 (166)	18.6 (167)	13.0 (169)
Enlisted Groundcrew	Ranch Hand	16.8 (394)	14.5 (380)	16.0 (375)	15.2 (394)
	Comparison	17.6 (471)	19.0 (458)	14.7 (457)	14.4 (471)

		Normal in 1982			
Occupational Category	Group	n in 1992	Percent High in 1992	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	*Ranch Hand*	*752*	*9.6*	*1.46 (1.02,2.10)*	*0.037*
	Comparison	*874*	*6.8*		
Officer	Ranch Hand	294	8.2	1.40 (0.76,2.57)	0.277
	Comparison	353	6.0		
Enlisted Flyer	Ranch Hand	130	12.3	2.20 (0.91,5.34)	0.081
	Comparison	133	6.0		
Enlisted Groundcrew	Ranch Hand	328	9.8	1.29 (0.77,2.18)	0.334
	Comparison	388	7.7		

[a] Relative risk, confidence interval, and p-values are in reference to a contrast of 1982 and 1992 results; results adjusted for age in 1992.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations. Statistical analyses are based only on participants who had a normal cholesterol level in 1982 (see Chapter 7, Statistical Methods).

Table 13-68. (Continued)
Longitudinal Analysis of Cholesterol
(Discrete)

b) MODEL 2: RANCH HANDS — INITIAL DIOXIN				
	Percent High/(n) Examination			
Initial Dioxin	1982	1985	1987	1992
Low	12.7 (166)	17.9 (162)	15.8 (165)	15.1 (166)
Medium	16.3 (166)	15.5 (161)	16.1 (162)	14.5 (166)
High	22.9 (166)	16.6 (163)	14.4 (160)	16.9 (166)

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
	Normal in 1982			
Initial Dioxin	n in 1992	Percent High in 1992	Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	145	9.7	1.05 (0.81,1.36)	0.717
Medium	139	7.9		
High	128	11.7		

[a] Adjusted for percent body fat at the time of duty in SEA, the change in percent body fat from the time of duty in SEA to the date of blood draw for dioxin, and age in 1992.

[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations. Statistical analyses are based only on participants who had a normal cholesterol level in 1982 (see Chapter 7, Statistical Methods).

Table 13-68. (Continued)
Longitudinal Analysis of Cholesterol
(Discrete)

c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY

	Percent High/(n) Examination			
Dioxin Category	**1982**	**1985**	**1987**	**1992**
Comparison	15.7 (896)	18.7 (884)	14.6 (883)	12.4 (896)
Background RH	11.0 (335)	14.8 (332)	17.3 (330)	12.8 (335)
Low RH	13.4 (247)	17.0 (241)	14.7 (245)	14.2 (247)
High RH	21.1 (251)	16.3 (245)	16.1 (242)	16.7 (251)
Low plus High RH	17.3 (498)	16.7 (486)	15.4 (487)	15.5 (498)

	Normal in 1982			
Dioxin Category	**n in 1992**	**Percent High in 1992**	**Adj. Relative Risk (95% C.I.)[ab]**	**p-Value[b]**
Comparison	755	6.6		
Background RH	298	9.4	1.43 (0.88,2.33)	0.152
Low RH	214	8.9	1.37 (0.79,2.38)	0.267
High RH	198	10.6	1.76 (1.02,3.03)	0.043
Low plus High RH	412	9.7	1.55 (1.00,2.40)	0.051

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA, the change in percent body fat from the time of duty in SEA to the date of blood draw for dioxin, and age in 1992.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤10 ppt.
Background (Ranch Hand): Current Dioxin ≤10 ppt.
Low (Ranch Hand): Current Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤143 ppt.
High (Ranch Hand): Current Dioxin >10 ppt, Initial Dioxin > 143 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations. Statistical analyses are based only on participants who had a normal cholesterol level in 1982 (see Chapter 7, Statistical Methods).

Table 13-69.
Longitudinal Analysis of HDL Cholesterol (mg/dl)
(Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS								
		Mean[a]/(n) Examination						
Occupational Category	Group	1982	1985	1987	1992	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
All	***Ranch Hand***	***44.18 (867)***	***44.44 (845)***	***45.29 (839)***	***40.58 (867)***	***-3.60***	***0.34***	***0.619***
	Comparison	***44.75 (1,029)***	***44.85 (1,005)***	***45.54 (999)***	***40.81 (1,029)***	***-3.94***		
Officer	Ranch Hand	45.77 (323)	45.97 (317)	46.80 (318)	42.20 (323)	-3.57	0.16	0.841
	Comparison	45.82 (395)	46.44 (387)	47.09 (381)	42.09 (395)	-3.73		
Enlisted Flyer	Ranch Hand	42.96 (154)	43.40 (152)	44.54 (149)	40.26 (154)	-2.70	0.20	0.849
	Comparison	43.11 (167)	43.23 (164)	44.34 (165)	40.21 (167)	-2.90		
Enlisted Groundcrew	Ranch Hand	43.39 (390)	43.60 (376)	44.34 (372)	39.42 (390)	-3.97	0.52	0.679
	Comparison	44.45 (467)	44.11 (454)	44.71 (453)	39.96 (467)	-4.49		

[a] Transformed from natural logarithm scale.

[b] Difference between 1992 and 1982 examination means after transformation to original scale.

[c] P-value is based on analysis of natural logarithm of HDL cholesterol; results adjusted for natural logarithm of HDL cholesterol in 1982 and age in 1992.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations.

Table 13-69. (Continued)
Longitudinal Analysis of HDL Cholesterol (mg/dl)
(Continuous)

b) MODEL 2: RANCH HANDS — INITIAL DIOXIN						
	Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]	
	Mean[a]/(n) Examination					
Initial Dioxin	1982	1985	1987	1992	Adj. Slope (Std. Error)	p-Value
Low	44.32 (165)	44.56 (161)	45.40 (164)	41.07 (165)	-0.002 (0.006)	0.796
Medium	42.32 (160)	42.19 (155)	42.84 (156)	38.87 (160)		
High	42.28 (161)	42.34 (158)	43.51 (156)	38.94 (161)		

[a] Transformed from natural logarithm scale.

[b] Results based on difference between natural logarithm of HDL cholesterol in 1992 and natural logarithm of HDL cholesterol in 1982 versus $\log_2$ (initial dioxin); results adjusted for percent body fat at the time of duty in SEA, the change in percent body fat from the time of duty in SEA to the date of blood draw for dioxin, natural logarithm of 1982 HDL cholesterol, and age in 1992.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations.

Table 13-69. (Continued)
Longitudinal Analysis of HDL Cholesterol (mg/dl)
(Continuous)

c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY							
	Mean[a]/(n) Examination						
Dioxin Category	1982	1985	1987	1992	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
Comparison	44.64 (888)	44.59 (876)	45.27 (875)	40.61 (888)	-4.04		
Background RH	45.80 (331)	46.36 (328)	47.46 (326)	42.38 (331)	-3.42	0.61	0.185
Low RH	44.20 (243)	44.18 (237)	44.92 (241)	40.69 (243)	-3.51	0.53	0.624
High RH	41.79 (243)	41.91 (237)	42.93 (235)	38.59 (243)	-3.20	0.84	0.502
Low plus High RH	42.98 (486)	43.03 (474)	43.93 (476)	39.63 (486)	-3.35	0.69	0.455

[a] Transformed from natural logarithm scale.

[b] Difference between 1992 and 1982 examination means after transformation to original scale.

[c] P-value is based on analysis of natural logarithm of HDL cholesterol; results adjusted for percent body fat at the time of duty in SEA, the change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, natural logarithm of HDL cholesterol in 1982, and age in 1992.

Note: RH = Ranch Hand.
Comparison: Current Dioxin $\leq$10 ppt.
Background (Ranch Hand): Current Dioxin $\leq$10 ppt.
Low (Ranch Hand): Current Dioxin >10 ppt, 10 ppt < Initial Dioxin $\leq$143 ppt.
High (Ranch Hand): Current Dioxin >10 ppt, Initial Dioxin >143 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations.

HDL Cholesterol (Discrete)

The longitudinal analysis for Model 1 did not reveal a significant group difference in the percentage of individuals with low HDL cholesterol for participants who had normal HDL cholesterol in 1982 (Table 13-70(a): $p>0.16$ for all contrasts). For Model 2, the longitudinal analysis did not show a significant association between initial dioxin and HDL cholesterol (Table 13-70(b): $p=0.950$). Examination of the Model 3 results did not reveal any of the Ranch Hand categories to be significantly different from the Comparison group (Table 13-70(c): $p>0.11$ for all contrasts).

In both the Ranch Hand and Comparison cohorts, the percentage of participants with low HDL cholesterol displayed a noticeable increase between 1987 and 1992. This increase may partially be attributed to a change in measurement procedure between the 1987 and 1992 examinations (ACA in 1987 versus Paramax® in 1992).

Cholesterol-HDL Ratio (Continuous)

The longitudinal analysis of Model 1 did not find a significant group difference in the means of the paired differences (Table 13-71(a): $p>0.37$ for all contrasts). Examination of the Model 2 results did not reveal a significant association between initial dioxin and the paired differences for cholesterol-HDL ratio (Table 13-71(b): $p=0.579$). For Model 3, the longitudinal analysis did not detect a significant difference between any of the Ranch Hand categories and Comparison group (Table 13-71(c): $p>0.45$ for all contrasts).

Cholesterol-HDL Ratio (Discrete)

The longitudinal analysis for Model 1 did not detect a significant group difference in the percentage of individuals with a high cholesterol-HDL ratio for participants who had a normal cholesterol-HDL ratio in 1982 (Table 13-72(a): $p>0.24$ for all contrasts). The Model 2 analysis did not reveal a significant association between initial dioxin and cholesterol-HDL ratio (Table 13-72(b): $p=0.879$). For Model 3, the longitudinal analysis did not show any of the Ranch Hand categories to be significantly different from the Comparison group (Table 13-72(c): $p>0.36$ for all contrasts).

In both the Ranch Hand and Comparison cohorts, the percentage of participants with a high cholesterol-HDL ratio showed a marked increase between 1987 and 1992. The change in measurement procedures between 1987 and 1992 (ACA in 1987 versus Paramax® in 1992) may have contributed to this increase. The 1987 and 1992 examinations used the same definition for a high cholesterol-HDL ratio.

Triglycerides (Continuous)

Examination of the paired differences in the longitudinal analysis of Model 1 did not show a significant group difference (Table 13-73(a): $p>0.13$ for all contrasts). The results for Model 2 did not reveal a significant association between initial dioxin and the paired differences for triglycerides (Table 13-73(b): $p=0.256$). The longitudinal analysis for Model 3 detected a marginally significant difference between the high Ranch Hands and the

Table 13-70.
Longitudinal Analysis of HDL Cholesterol
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS					
		Percent Low/(n) Examination			
Occupational Category	Group	1982	1985	1987	1992
All	*Ranch Hand*	*3.1 (867)*	*4.1 (845)*	*2.9 (839)*	*11.0 (867)*
	Comparison	*1.9 (1,029)*	*4.0 (1,005)*	*2.3 (999)*	*8.5 (1,029)*
Officer	Ranch Hand	3.4 (323)	4.7 (317)	3.5 (318)	11.2 (323)
	Comparison	2.5 (395)	3.9 (387)	1.3 (381)	7.9 (395)
Enlisted Flyer	Ranch Hand	3.3 (154)	5.3 (152)	4.0 (149)	9.1 (154)
	Comparison	1.8 (167)	5.5 (164)	3.6 (165)	9.6 (167)
Enlisted Groundcrew	Ranch Hand	2.8 (390)	3.2 (376)	1.9 (372)	11.5 (390)
	Comparison	1.3 (467)	3.5 (454)	2.7 (453)	8.6 (467)

		Normal in 1982			
Occupational Category	Group	n in 1992	Percent Low in 1992	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	*Ranch Hand*	*840*	*9.6*	*1.26 (0.91,1.74)*	*0.167*
	Comparison	*1,010*	*7.8*		
Officer	Ranch Hand	312	9.6	1.47 (0.85,2.54)	0.170
	Comparison	385	6.8		
Enlisted Flyer	Ranch Hand	149	8.1	0.87 (0.39,1.93)	0.731
	Comparison	164	9.2		
Enlisted Groundcrew	Ranch Hand	379	10.3	1.28 (0.80,2.05)	0.305
	Comparison	461	8.2		

[a] Relative risk, confidence interval, and p-values are in reference to a contrast of 1982 and 1992 results; results adjusted for age in 1992.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations. Statistical analyses are based only on participants who had a normal HDL cholesterol level in 1982 (see Chapter 7, Statistical Methods).

Table 13-70. (Continued)
Longitudinal Analysis of HDL Cholesterol
(Discrete)

b) MODEL 2: RANCH HANDS — INITIAL DIOXIN				
	Percent Low/(n) Examination			
Initial Dioxin	1982	1985	1987	1992
Low	3.0 (165)	3.7 (161)	1.2 (164)	7.9 (165)
Medium	3.8 (160)	5.8 (155)	2.6 (156)	12.5 (160)
High	1.9 (161)	4.4 (158)	2.6 (156)	11.2 (161)

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
	Normal in 1982			
Initial Dioxin	n in 1992	Percent Low in 1992	Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	160	7.5	0.99 (0.77,1.27)	0.950
Medium	154	10.4		
High	158	9.5		

[a] Adjusted for percent body fat at the time of duty in SEA, the change in percent body fat from the time of duty in SEA to the date of blood draw for dioxin, and age in 1992.

[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations. Statistical analyses are based only on participants who had a normal HDL cholesterol level in 1982 (see Chapter 7, Statistical Methods).

Table 13-70. (Continued)
Longitudinal Analysis of HDL Cholesterol
(Discrete)

c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY				
	Percent Low/(n) Examination			
Dioxin Category	1982	1985	1987	1992
Comparison	1.7 (888)	4.2 (876)	2.4 (875)	8.3 (888)
Background RH	3.3 (331)	3.4 (328)	3.7 (326)	10.3 (331)
Low RH	3.7 (243)	5.1 (237)	1.7 (241)	9.1 (243)
High RH	2.1 (243)	4.2 (237)	2.6 (235)	11.9 (243)
Low plus High RH	2.9 (486)	4.6 (474)	2.1 (476)	10.5 (486)

	Normal in 1982			
Dioxin Category	n in 1992	Percent Low in 1992	Adj. Relative Risk (95% C.I.)[ab]	p-Value[b]
Comparison	873	7.7		
Background RH	320	9.1	1.46 (0.91,2.32)	0.115
Low RH	234	8.1	1.03 (0.60,1.77)	0.914
High RH	238	10.1	1.16 (0.70,1.92)	0.567
Low plus High RH	472	9.1	1.10 (0.73,1.65)	0.657

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA, the change in percent body fat from the time of duty in SEA to the date of blood draw for dioxin, and age in 1992.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤10 ppt.
Background (Ranch Hand): Current Dioxin ≤10 ppt.
Low (Ranch Hand): Current Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤143 ppt.
High (Ranch Hand): Current Dioxin >10 ppt, Initial Dioxin > 143 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations. Statistical analyses are based only on participants who had a normal HDL cholesterol level in 1982 (see Chapter 7, Statistical Methods).

Table 13-71.
Longitudinal Analysis of Cholesterol-HDL Ratio (Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS								
		Mean[a]/(n) Examination						
Occupational Category	Group	1982	1985	1987	1992	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
All	*Ranch Hand*	*4.77 (867)*	*4.81 (845)*	*4.72 (839)*	*5.28 (867)*	*0.52*	*0.05*	*0.375*
	Comparison	*4.78 (1,029)*	*4.81 (1,005)*	*4.70 (999)*	*5.25 (1,029)*	*0.47*		
Officer	Ranch Hand	4.62 (323)	4.67 (317)	4.57 (318)	5.05 (323)	0.42	0.06	0.456
	Comparison	4.64 (395)	4.62 (387)	4.53 (381)	5.01 (395)	0.37		
Enlisted Flyer	Ranch Hand	4.99 (154)	5.01 (152)	4.82 (149)	5.38 (154)	0.39	0.07	0.839
	Comparison	5.17 (167)	5.10 (164)	4.98 (165)	5.48 (167)	0.32		
Enlisted Groundcrew	Ranch Hand	4.80 (390)	4.85 (376)	4.81 (372)	5.45 (390)	0.65	0.04	0.608
	Comparison	4.77 (467)	4.86 (454)	4.75 (453)	5.37 (467)	0.61		

[a] Transformed from natural logarithm scale.

[b] Difference between 1992 and 1982 examination means after transformation to original scale.

[c] P-value is based on analysis of natural logarithm of cholesterol-HDL ratio; results adjusted for natural logarithm of cholesterol-HDL ratio in 1982 and age in 1992.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations.

Table 13-71. (Continued)
Longitudinal Analysis of Cholesterol-HDL Ratio
(Continuous)

b) MODEL 2: RANCH HANDS — INITIAL DIOXIN						
	Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]	
	Mean[a]/(n) Examination					
Initial Dioxin	1982	1985	1987	1992	Adj. Slope (Std. Error)	p-Value
Low	4.79 (165)	4.85 (161)	4.74 (164)	5.25 (165)	0.004 (0.007)	0.579
Medium	4.97 (160)	5.09 (155)	4.99 (156)	5.49 (160)		
High	5.06 (161)	5.09 (158)	4.99 (156)	5.56 (161)		

[a] Transformed from natural logarithm scale.

[b] Results based on difference between natural logarithm of cholesterol-HDL ratio in 1992 and natural logarithm of cholesterol-HDL ratio in 1982 versus log_2 (initial dioxin); results adjusted for percent body fat at the time of duty in SEA, the change in percent body fat from the time of duty in SEA to the date of blood draw for dioxin, natural logarithm of 1982 cholesterol-HDL ratio, and age in 1992.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations.

Table 13-71. (Continued)
Longitudinal Analysis of Cholesterol-HDL Ratio
(Continuous)

c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY							
	Mean[a]/(n) Examination						
Dioxin Category	1982	1985	1987	1992	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
Comparison	4.81 (888)	4.85 (876)	4.75 (875)	5.28 (888)	0.47		
Background RH	4.54 (331)	4.55 (328)	4.46 (326)	5.03 (331)	0.49	0.02	0.902
Low RH	4.78 (243)	4.86 (237)	4.75 (241)	5.25 (243)	0.47	0.00	0.707
High RH	5.09 (243)	5.17 (237)	5.07 (235)	5.62 (243)	0.53	0.06	0.452
Low plus High RH	4.93 (486)	5.01 (474)	4.91 (476)	5.43 (486)	0.50	0.03	0.469

[a] Transformed from natural logarithm scale.

[b] Difference between 1992 and 1982 examination means after transformation to original scale.

[c] P-value is based on analysis of natural logarithm of cholesterol-HDL ratio; results adjusted for percent body fat at the time of duty in SEA, the change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, natural logarithm of cholesterol-HDL ratio in 1982, and age in 1992.

Note: RH = Ranch Hand.
Comparison: Current Dioxin $\leq$10 ppt.
Background (Ranch Hand): Current Dioxin $\leq$10 ppt.
Low (Ranch Hand): Current Dioxin >10 ppt, 10 ppt < Initial Dioxin $\leq$143 ppt.
High (Ranch Hand): Current Dioxin >10 ppt, Initial Dioxin >143 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations.

Table 13-72.
Longitudinal Analysis of Cholesterol-HDL Ratio (Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS					
		Percent High/(n) Examination			
Occupational Category	Group	1982	1985	1987	1992
All	*Ranch Hand*	*45.8 (867)*	*45.8 (845)*	*43.4 (839)*	*58.6 (867)*
	Comparison	*44.6 (1,029)*	*44.4 (1,005)*	*42.8 (999)*	*57.1 (1,029)*
Officer	Ranch Hand	39.6 (323)	44.2 (317)	40.9 (318)	50.5 (323)
	Comparison	41.5 (395)	38.5 (387)	36.8 (381)	49.1 (395)
Enlisted Flyer	Ranch Hand	51.3 (154)	47.4 (152)	42.3 (149)	64.3 (154)
	Comparison	56.3 (167)	51.2 (164)	53.9 (165)	63.5 (167)
Enlisted Groundcrew	Ranch Hand	48.7 (390)	46.5 (376)	46.0 (372)	63.1 (390)
	Comparison	43.0 (467)	46.9 (454)	43.9 (453)	61.5 (467)

		Normal in 1982			
Occupational Category	Group	n in 1992	Percent High in 1992	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	*Ranch Hand*	*470*	*34.5*	*0.93 (0.72,1.20)*	*0.570*
	Comparison	*570*	*36.1*		
Officer	Ranch Hand	195	29.2	0.99 (0.65,1.51)	0.969
	Comparison	231	29.4		
Enlisted Flyer	Ranch Hand	75	42.7	1.26 (0.65,2.43)	0.497
	Comparison	73	37.0		
Enlisted Groundcrew	Ranch Hand	200	36.5	0.80 (0.55,1.17)	0.246
	Comparison	266	41.7		

[a] Relative risk, confidence interval, and p-values are in reference to a contrast of 1982 and 1992 results; results adjusted for age in 1992.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations. Statistical analyses are based only on participants who had a normal cholesterol-HDL ratio level in 1982 (see Chapter 7, Statistical Methods).

Table 13-72. (Continued)
Longitudinal Analysis of Cholesterol-HDL Ratio (Discrete)

b) MODEL 2: RANCH HANDS — INITIAL DIOXIN				
	Percent High/(n) Examination			
Initial Dioxin	1982	1985	1987	1992
Low	44.2 (165)	46.6 (161)	43.9 (164)	56.4 (165)
Medium	50.0 (160)	50.3 (155)	50.0 (156)	68.1 (160)
High	54.7 (161)	53.8 (158)	50.0 (156)	63.4 (161)

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
	Normal in 1982			
Initial Dioxin	n in 1992	Percent High in 1992	Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	92	29.4	1.02 (0.82,1.26)	0.879
Medium	80	45.0		
High	73	34.3		

[a] Adjusted for percent body fat at the time of duty in SEA, the change in percent body fat from the time of duty in SEA to the date of blood draw for dioxin, and age in 1992.

[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations. Statistical analyses are based only on participants who had a normal cholesterol-HDL ratio level in 1982 (see Chapter 7, Statistical Methods).

Table 13-72. (Continued)
Longitudinal Analysis of Cholesterol-HDL Ratio
(Discrete)

c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY

Dioxin Category	Percent High/(n) Examination 1982	1985	1987	1992
Comparison	44.4 (888)	44.9 (876)	43.7 (875)	57.9 (888)
Background RH	39.3 (331)	39.6 (328)	35.6 (326)	52.0 (331)
Low RH	43.6 (243)	44.7 (237)	43.6 (241)	58.4 (243)
High RH	55.6 (243)	55.7 (237)	52.3 (235)	66.7 (243)
Low plus High RH	49.6 (486)	50.2 (474)	47.9 (476)	62.6 (486)

Dioxin Category	Normal in 1982: n in 1992	Normal in 1982: Percent High in 1992	Adj. Relative Risk (95% C.I.)[ab]	p-Value[b]
Comparison	494	37.3		
Background RH	201	32.8	0.88 (0.61,1.25)	0.463
Low RH	137	33.6	0.83 (0.55,1.24)	0.361
High RH	108	38.9	0.97 (0.63,1.50)	0.894
Low plus High RH	245	35.9	0.89 (0.64,1.23)	0.477

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA, the change in percent body fat from the time of duty in SEA to the date of blood draw for dioxin, and age in 1992.

Note: RH = Ranch Hand.
Comparison: Current Dioxin $\leq$10 ppt.
Background (Ranch Hand): Current Dioxin $\leq$10 ppt.
Low (Ranch Hand): Current Dioxin >10 ppt, 10 ppt < Initial Dioxin $\leq$143 ppt.
High (Ranch Hand): Current Dioxin >10 ppt, Initial Dioxin > 143 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations. Statistical analyses are based only on participants who had a normal cholesterol-HDL ratio level in 1982 (see Chapter 7, Statistical Methods).

Table 13-73.
Longitudinal Analysis of Triglycerides (mg/dl)
(Continuous)

a) MODEL 1: RANCH HANDS VS. COMPARISONS								
		Mean[a]/(n) Examination						
Occupational Category	Group	1982	1985	1987	1992	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
All	*Ranch Hand*	*121.48 (884)*	*118.37 (862)*	*120.17 (855)*	*147.67 (884)*	*26.19*	*2.31*	*0.426*
	Comparison	*121.28 (1,038)*	*118.82 (1,014)*	*119.34 (1,008)*	*145.15 (1,038)*	*23.88*		
Officer	Ranch Hand	121.44 (332)	118.30 (326)	117.57 (327)	145.03 (332)	23.58	3.65	0.196
	Comparison	116.23 (398)	111.38 (390)	111.19 (384)	136.17 (398)	19.93		
Enlisted Flyer	Ranch Hand	130.14 (158)	122.02 (156)	123.02 (153)	145.21 (158)	15.07	-8.83	0.136
	Comparison	134.76 (169)	131.86 (166)	131.51 (167)	158.66 (169)	23.90		
Enlisted Groundcrew	Ranch Hand	118.21 (394)	116.95 (380)	121.33 (375)	150.95 (394)	32.74	5.40	0.358
	Comparison	121.04 (471)	120.89 (458)	122.23 (457)	148.39 (471)	27.35		

[a] Transformed from natural logarithm scale.

[b] Difference between 1992 and 1982 examination means after transformation to original scale.

[c] P-value is based on analysis of natural logarithm of triglycerides; results adjusted for natural logarithm of triglycerides in 1982 and age in 1992.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations.

Table 13-73. (Continued)
Longitudinal Analysis of Triglycerides (mg/dl)
(Continuous)

b) MODEL 2: RANCH HANDS — INITIAL DIOXIN						
	Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]	
	Mean[a]/(n) Examination					
Initial Dioxin	1982	1985	1987	1992	Adj. Slope (Std. Error)	p-Value
Low	126.17 (166)	121.03 (162)	119.56 (165)	144.39 (166)	0.018 (0.015)	0.256
Medium	130.57 (166)	130.43 (161)	142.55 (162)	164.49 (166)		
High	134.61 (166)	135.79 (163)	136.50 (160)	164.77 (166)		

[a] Transformed from natural logarithm scale.

[b] Results based on difference between natural logarithm of triglycerides in 1992 and natural logarithm of triglycerides in 1982 versus log_2 (initial dioxin); results adjusted for percent body fat at the time of duty in SEA, the change in percent body fat from the time of duty in SEA to the date of blood draw for dioxin, natural logarithm of 1982 triglycerides, and age in 1992.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations.

Table 13-73. (Continued)
Longitudinal Analysis of Triglycerides (mg/dl)
(Continuous)

c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY							
	Mean[a]/(n) Examination						
Dioxin Category	1982	1985	1987	1992	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
Comparison	122.65 (896)	119.82 (884)	121.62 (883)	146.71 (896)	24.07		
Background RH	109.10 (335)	104.81 (332)	104.41 (330)	132.74 (335)	23.64	-0.43	0.462
Low RH	125.29 (247)	122.98 (241)	123.36 (245)	147.77 (247)	22.48	-1.58	0.956
High RH	135.65 (251)	135.11 (245)	142.23 (242)	167.88 (251)	32.24	8.17	0.056
Low plus High RH	130.41 (498)	128.95 (486)	132.40 (487)	157.59 (498)	27.18	3.11	0.207

[a] Transformed from natural logarithm scale.

[b] Difference between 1992 and 1982 examination means after transformation to original scale.

[c] P-value is based on analysis of natural logarithm of triglycerides; results adjusted for percent body fat at the time of duty in SEA, the change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, natural logarithm of triglycerides in 1982, and age in 1992.

Note: RH = Ranch Hand.
Comparison: Current Dioxin $\leq$10 ppt.
Background (Ranch Hand): Current Dioxin $\leq$10 ppt.
Low (Ranch Hand): Current Dioxin >10 ppt, 10 ppt < Initial Dioxin $\leq$143 ppt.
High (Ranch Hand): Current Dioxin >143 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations.

Comparison group (Table 13-73(c): $p=0.056$). The mean paired difference was greater for the high Ranch Hands than the Comparison group (32.24 mg/dl vs. 24.07 mg/dl).

Triglycerides (Discrete)

The longitudinal analysis for Model 1 did not reveal a significant group difference in the percentage of individuals with high levels of triglycerides for participants who had normal levels of triglycerides at the 1982 examination (Table 13-74(a): $p>0.36$ for all contrasts). For Model 2, the longitudinal analysis did not detect a significant association between initial dioxin and triglycerides (Table 13-74(b): $p=0.587$). Examination of the Model 3 results did not show any of the Ranch Hand categories to be significantly different from the Comparison group (Table 13-74(c): $p>0.43$ for all contrasts).

In both the Ranch Hand and Comparison cohorts, the percentage of participants with high measurements of triglycerides showed a marked decrease between 1982 and 1985 and a noticeable increase between 1987 and 1992. The decrease between 1982 and 1985 may partly be attributed to a change in the definition of a high triglyceride level between 1982 and 1985. For example, for participants less than 40 years of age in 1982, a high triglyceride level was greater than 150 mg/dl, whereas the 1985 examination defined a high triglyceride level as greater than 320 mg/dl. The increase between 1987 and 1992 may have been caused by a change in the measurement technique (ACA in 1987 versus Paramax® in 1992).

DISCUSSION

Signs and symptoms associated with the gastrointestinal system are encountered frequently in ambulatory medicine. The historical, physical examination, and laboratory parameters included in the gastrointestinal assessment are well established in clinical practice as screening tools in the outpatient investigation of digestive disorders.

It is important to recognize the limitations of relying on data from the patient history and physical examination when diagnosing digestive disorders. Rather than pointing to a particular diagnosis, digestive symptoms frequently are nonspecific and intermittent. In this setting, even the best designed medical history questionnaire can be subject to error. "Ulcer" and "colitis" are diagnoses that are commonly reported but often not accurately established. As a common target organ for situational stress, the bowel frequently gives rise to symptoms that can be severe but that are functional in nature and resolve over time. These caveats highlight the importance of the type of medical record verification conducted in the current study and, in the case of hepatitis, the need for serologic confirmation.

The physical examination of the gastrointestinal system is often of limited value and can be misleading in the differential diagnosis. For example, detecting hepatomegaly in the obese patient is unreliable. In obstructive airway disease, with hyperinflation of the lungs and flattening of the diaphragms, the liver edge may descend abnormally below the right costal margin in the absence of hepatomegaly. Even in the best circumstance, the span of the liver by palpation or percussion is often an unreliable index of liver size.

Table 13-74.
Longitudinal Analysis of Triglycerides
(Discrete)

a) MODEL 1: RANCH HANDS VS. COMPARISONS					
		Percent High/(n) Examination			
Occupational Category	Group	1982	1985	1987	1992
All	***Ranch Hand***	***31.7 (884)***	***7.3 (862)***	***7.3 (855)***	***11.4 (884)***
	Comparison	***32.6 (1,038)***	***6.3 (1,014)***	***6.6 (1,008)***	***9.5 (1,038)***
Officer	Ranch Hand	28.6 (332)	10.1 (326)	7.6 (327)	12.1 (332)
	Comparison	29.7 (398)	5.9 (390)	6.8 (384)	8.3 (398)
Enlisted Flyer	Ranch Hand	37.3 (158)	9.0 (156)	7.2 (153)	13.3 (158)
	Comparison	37.3 (169)	6.6 (166)	6.6 (167)	11.2 (169)
Enlisted Groundcrew	Ranch Hand	32.0 (394)	4.2 (380)	6.9 (375)	10.2 (394)
	Comparison	33.3 (471)	6.6 (458)	6.4 (457)	10.0 (471)

		Normal in 1982			
Occupational Category	Group	n in 1992	Percent High in 1992	Adj. Relative Risk (95% C.I.)[a]	p-Value[a]
All	***Ranch Hand***	***604***	***2.8***	***1.12 (0.57,2.19)***	***0.749***
	Comparison	***700***	***2.6***		
Officer	Ranch Hand	237	3.0	1.72 (0.54,5.50)	0.361
	Comparison	280	1.8		
Enlisted Flyer	Ranch Hand	99	1.0	0.36 (0.04,3.52)	0.377
	Comparison	106	2.8		
Enlisted Groundcrew	Ranch Hand	268	3.4	1.10 (0.44,2.75)	0.838
	Comparison	314	3.2		

[a] Relative risk, confidence interval, and p-values are in reference to a contrast of 1982 and 1992 results; results adjusted for age in 1992.

Note: Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations. Statistical analyses are based only on participants who had a normal triglycerides level in 1982 (see Chapter 7, Statistical Methods).

Table 13-74. (Continued)
Longitudinal Analysis of Triglycerides
(Discrete)

b) MODEL 2: RANCH HANDS — INITIAL DIOXIN				
	Percent High/(n) Examination			
Initial Dioxin	1982	1985	1987	1992
Low	33.7 (166)	8.6 (162)	5.5 (165)	9.6 (166)
Medium	36.1 (166)	9.9 (161)	9.9 (162)	16.9 (166)
High	39.2 (166)	8.0 (163)	12.5 (160)	13.3 (166)

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
	Normal in 1982			
Initial Dioxin	n in 1992	Percent High in 1992	Adj. Relative Risk (95% C.I.)[b]	p-Value
Low	110	2.7	1.13 (0.73,1.74)	0.587
Medium	106	6.6		
High	101	2.0		

[a] Adjusted for percent body fat at the time of duty in SEA, the change in percent body fat from the time of duty in SEA to the date of blood draw for dioxin, and age in 1992.

[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations. Statistical analyses are based only on participants who had a normal triglycerides level in 1982 (see Chapter 7, Statistical Methods).

Table 13-74. (Continued)
Longitudinal Analysis of Triglycerides
(Discrete)

c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY				
	Percent High/(n) Examination			
Dioxin Category	1982	1985	1987	1992
Comparison	33.4 (896)	6.6 (884)	7.1 (883)	9.7 (896)
Background RH	24.2 (335)	4.5 (332)	4.6 (330)	8.7 (335)
Low RH	34.8 (247)	9.5 (241)	7.4 (245)	11.3 (247)
High RH	37.9 (251)	8.2 (245)	11.2 (242)	15.1 (251)
Low plus High RH	36.4 (498)	8.9 (486)	9.2 (487)	13.3 (498)

	Normal in 1982			
Dioxin Category	n in 1992	Percent High in 1992	Adj. Relative Risk (95% C.I.)[ab]	p-Value[b]
Comparison	597	3.0		
Background RH	254	2.0	0.72 (0.26,1.99)	0.529
Low RH	161	3.1	0.91 (0.33,2.51)	0.850
High RH	156	4.5	1.44 (0.58,3.61)	0.432
Low plus High RH	317	3.8	1.15 (0.54,2.46)	0.709

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA, the change in percent body fat from the time of duty in SEA to the date of blood draw for dioxin, and age in 1992.

Note: RH = Ranch Hand.
Comparison: Current Dioxin $\leq$10 ppt.
Background (Ranch Hand): Current Dioxin $\leq$10 ppt.
Low (Ranch Hand): Current Dioxin >10 ppt, 10 ppt < Initial Dioxin $\leq$143 ppt.
High (Ranch Hand): Current Dioxin >10 ppt, Initial Dioxin > 143 ppt.
Summary statistics for 1985 are provided for reference purposes for participants who attended the Baseline, 1985, and 1992 examinations. Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations. Statistical analyses are based only on participants who had a normal triglycerides level in 1982 (see Chapter 7, Statistical Methods).

Although there are limitations to the history and physical examination, data collected in the laboratory can provide early insight into the presence of occult liver disease. The four hepatic enzymes analyzed as dependent variables (AST, ALT, GGT, and LDH) are commonly ordered in the outpatient setting. Present in high intracellular concentration, these enzymes, of which GGT is the most sensitive, are released in virtually all toxic, inflammatory and neoplastic diseases with hepatic involvement.

The hepatic enzymes are used in the detection and followup of parenchymal liver disease. The serum alkaline phosphatase and bilirubin are reflective of hepatobiliary function and are elevated in "cholestatic" or "obstructive" diseases. Although present in virtually all organ systems, the serum alkaline phosphatase in the adult population under study is of dual origin and close to a 50-50 mixture of liver- and bone-derived fractions. An elevated alkaline phosphatase is by no means diagnostic of liver disease. An elevated alkaline phosphatase level may occur in a broad range of unrelated clinical conditions including drug-induced cholestasis, Paget's disease (3% of males over age 40), neoplasia with metastases to bone, and congestive heart failure.

Similarly, the bilirubin measurements are subject to numerous hereditary and acquired disorders unrelated to intrinsic hepatic disease. The benign hyperbilirubinemia of Gilbert's syndrome will occur in 5 percent of the population under study. Many medications, including over-the-counter preparations, have been implicated in the overproduction of bilirubin in the hemolytic reactions associated with glucose-6-phosphate dehydrogenase deficiency, which may occur in up to 15 percent of Black American males.

In the current assessment, analysis of the historical and clinical examination variables revealed no evidence of any overt hepatic disease related to the current body burden of dioxin. Most of the statistically significant associations that occurred in relation to the extrapolated initial level of serum dioxin were limited to the laboratory indices. With the exceptions noted below, these associations were found in the continuous, rather than the more clinically relevant discrete, analysis. While the observed dose-response findings are not accompanied by clinical disease, they may still represent subclinical effects.

With a few exceptions, the history of digestive diseases documented by medical record review was similar in the Ranch Hand and Comparison cohorts. Ranch Hands were less likely than Comparisons to have a history of jaundice (1.8% vs. 3.0%), a finding that is consistent with the highly significant ($p<0.001$) inverse dose-response effect found in all models relating this covariate to current serum dioxin. In contrast, a positive dose-response was noted in Ranch Hands who were more likely than Comparisons to have a history of "other liver disorders" (30.1% vs. 27.9%), a combination of ICD categories that included 4 participants with unspecified liver disorders and 637 participants with nonspecific laboratory test elevations at earlier AFHS physical examinations.

The laboratory data examined can be divided broadly into parenchymal (serum enzymes), hepatobillar (serum bilirubin and alkaline phosphatase), lipid/carbohydrate indices, and a 10-element protein profile including prealbumin, albumin, α-1-acid glycoprotein, α-1 antitrypsin, α-2 macroglobulin, apoliprotein B, C_3 complement, C_4 complement haptoglobin, and transferrin. The components of the protein profile were selected to provide a

comprehensive, if nonspecific, reflection of multiple organ systems involved in homeostasis and to rule out a subclinical inflammatory process that might be associated with prior TCDD exposure or the current body burden of dioxin. Produced in the liver, the proteins measured are most sensitive to hepatic function but also provide a reliable assessment of nutritional status. Selected proteins (α-1 acid glycoprotein, α-1 antitrypsin, and haptoglobin) are nonspecifically elevated in association with inflammation, whereas reductions in the C_3 and C_4 complement indices are associated with immune system responses.

Few of the laboratory analyses revealed any significant differences between Ranch Hand and Comparison cohorts. Ranch Hands had a slightly higher mean alkaline phosphatase than Comparisons but the difference in the means (70.73 U/L vs. 68.55 U/L) cannot be considered biologically significant, and both were within the range of normal. In the clinically more relevant analyses in discrete form, and in contrast to the 1985 and 1987 examinations, no significant group differences were defined in the current assessment. The TCDD-associated elevations in C_3 complement seen in these analyses are consistent with elevations in C_3 complement seen in diabetics, a condition also associated with TCDD exposure (see Chapter 18).

Several of the analyses yielded results that have been documented in prior examinations. In continuous, but not in discrete form, two of the four liver enzymes studied, ALT and GGT, revealed highly significant positive associations with current serum dioxin levels in statistical models using current TCDD levels. Similar results were noted with serum triglycerides and, in one of the models, serum cholesterol as well. The negative association of HDL cholesterol with current serum dioxin contributed to the highly significant cholesterol/HDL ratio results. Though these findings are similar to those reported in the 1992 serum dioxin analysis and consistent with a dose-response effect, a causal relationship remains to be established.

Dependent variable-covariate associations yielded results similar to those documented during the 1987 examinations and well established in clinical practice. Highly significant ($p<0.001$) positive correlations were noted relating lifetime alcohol consumption and a host of variables including the incidence over time of chronic liver disease, cirrhosis, and hepatomegaly and in the laboratory, elevations in HDL cholesterol and the hepatic enzymes AST and GGT. The mean creatine kinase level in Blacks was almost twice than in non-Blacks (233.07 U/L vs. 124.27 U/L), a finding that was noted in 1987 and that appears to be race- and gender-specific.

Over a decade of observation, the longitudinal analyses yielded significant results in several of the laboratory indices. Though no significant group differences were defined, a consistent, gradual reduction in serum AST occurred in Comparisons and Ranch Hands across all occupational and exposure categories. In the analyses of ALT in discrete form, Ranch Hands with a normal result in 1982 are now less likely than Comparisons to have an elevated ALT level and the reduction in risk was most apparent in the enlisted groundcrew stratum (4.1% vs. 7.3%). Relative to Comparisons, the increase in mean serum triglyceride levels over time was most pronounced in Ranch Hands in the highest serum dioxin category (32.34 mg/dl vs. 24.27 mg/dl). Finally, by discrete analyses, Ranch Hands were more likely than Comparisons to develop higher cholesterol over time (9.5% vs. 6.7%). Although these

results are consistent with a subtle effect of herbicide exposure on lipid metabolism, the adjusted relative risk was more pronounced in the enlisted flyer category than in the more highly exposed enlisted groundcrew category.

In summary, data analyzed in the current section confirm observations that would be anticipated in a clinical practice and reflect no apparent increase in organ-specific morbidity in Ranch Hands relative to Comparisons. Although a subclinical dioxin effect on lipid metabolism cannot be excluded, some of the results may be related in part to body habitus and percent body fat.

SUMMARY

Tables 13-75 through 13-78 summarize the results of the group contrast analyses (Table 13-75), the initial dioxin analyses (Table 13-76), the categorized dioxin analyses (Table 13-77) and the current dioxin analyses (Table 13-78). Table 13-79 lists the numerous group-by covariate and dioxin-by covariate interactions that were encountered in the adjusted analyses of the variables.

Analyses of data collected at the 1987 followup study indicated that dioxin was associated with military occupation. Adjustment for military occupation may improperly mask an actual dioxin effect, but occupation can also be a surrogate for important socioeconomic effects. If occupation was found to be significantly associated with a dependent variable in the 1992 followup analyses and was retained in the final statistical models using dioxin as an estimate of exposure, the dioxin effect was evaluated in the context of two models. Analyses were performed both with and without occupation in the models to investigate whether conclusions differ regarding the association between the health endpoint and dioxin. Examination of these contrasts revealed that for several variables, the serum dioxin analyses showed contradictory results depending on whether or not the occupation covariate was included in the final adjusted model. In most of these instances the results were nonsignificant when occupation was included in the final adjusted model, and became significant after excluding occupation. These differences most probably reflect the confounding effects of occupation, which was highly associated both with serum dioxin levels and many of the dependent variables.

An alternative explanation is that the results with occupation in the model were not significant because of collinearity between serum dioxin levels and occupation. Collinearity would cause the standard error of the estimates to increase, thus leading to a less significant result. However, this interpretation is less likely, because examination of the corresponding pairs of results shows that significance changes were primarily associated with changes in the relative risk and slope estimates (an expected effect of confounding), and only minimally associated with increases in the standard error of the estimates.

Table 13-75.
Summary of Group Analyses (Model 1) for Gastrointestinal Variables (Ranch Hands vs. Comparisons)

	UNADJUSTED			
Variable	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Medical Records				
Hepatitis (Non-A, Non-B, and Non-C) (D)	NS	NS	NS	ns
Jaundice (D)	ns	ns	NS	ns*
Chronic Liver Disease and Cirrhosis (Alcohol-Related) (D)	NS	NS	ns	ns
Chronic Liver Disease and Cirrhosis (Nonalcohol-Related) (D)	NS	NS	NS	NS
Other Liver Disorders (D)	NS	NS	ns	NS
Hepatomegaly (D)	ns	ns	NS	ns*
Physical Examination				
Current Hepatomegaly (D)	ns	ns	--	ns
Laboratory				
AST (C)	ns	ns	-0.022	ns
AST (D)	ns	ns	ns	ns
ALT (C)	-0.047	ns	-0.010	ns
ALT (D)	ns	ns	ns	ns
GGT (C)	NS	NS	ns	NS
GGT (D)	NS	NS	ns	NS
Alkaline Phosphatase (C)	+0.005	NS	ns	+0.001
Alkaline Phosphatase (D)	+0.039	NS	ns	+0.007
Total Bilirubin (C)	ns	NS	ns	ns
Total Bilirubin (D)	NS	NS	ns	NS
Direct Bilirubin (D)	ns	NS	ns	-0.022
LDH (C)	NS	ns	ns	NS
LDH (D)	NS	ns	ns	NS
Cholesterol (C)	NS	NS	ns	NS
Cholesterol (D)	NS	NS	NS	NS
HDL Cholesterol (C)[a]	ns	ns	NS	ns
HDL Cholesterol (D)	NS*	NS*	ns	NS
Cholesterol-HDL Ratio (C)	NS	NS	ns	NS
Cholesterol-HDL Ratio (D)	NS	NS	ns	NS
Triglycerides (C)	NS	NS*	ns*	NS
Triglycerides (D)	NS	NS*	NS	ns
Creatine Kinase (C)	ns	NS	ns	ns
Creatine Kinase (D)	NS	NS	ns	NS
Serum Amylase (C)	ns	ns	NS	NS
Serum Amylase (D)	ns	ns	NS	NS

Table 13-75. (Continued)
Summary of Group Analyses (Model 1) for Gastrointestinal Variables (Ranch Hands vs. Comparisons)

	UNADJUSTED			
Variable	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Antibodies for Hepatitis A (D)	ns	NS	NS	ns
Serological Evidence of Prior Hepatitis B Infection (D)	-0.001	-0.030	ns*	ns*
Antibodies for Hepatitis C (D)	ns*	ns	--	ns
Stool Hemoccult (D)	NS	NS	--	NS
Prealbumin (C)[a]	ns	NS	ns	ns
Prealbumin (D)	NS	ns	NS	NS
Albumin (C)[a]	ns	ns	ns	ns
Albumin (D)	NS	NS	ns	NS
α-1 Acid Glycoprotein (C)	NS	ns	NS	NS
α-1 Acid Glycoprotein (D)	ns	ns	NS	ns
α-1 Antitrypsin (C)	NS*	NS	NS	NS
α-1 Antitrypsin (D): Low vs. Normal	NS	NS	NS	NS
α-1 Antitrypsin (C): High vs. Normal	NS	NS	NS	NS
α-2 Macroglobulin (C)	ns	ns	ns	NS
α-2 Macroglobulin (D)	ns	--	ns	NS
Apolipoprotein B (C)	ns	ns	ns	NS
Apolipoprotein B (D)	NS	NS	ns	NS
C_3 Complement (C)[a]	ns	NS	ns	ns
C_3 Complement (D)	NS	ns	ns	NS
C_4 Complement (C)[a]	ns	ns	NS	ns
C_4 Complement (D)	ns	NS	ns	NS
Haptoglobin (C)	+0.004	NS	NS	+0.015
Haptoglobin (D)	NS	NS	NS	NS
Transferrin (C)[a]	+0.042	NS	ns	+0.016
Transferrin (D)	ns	ns	NS	ns

[a] Negative difference considered adverse for this variable.

C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥ 1.00 for discrete analysis or difference of means nonnegative for continuous analysis.
-: Relative risk < 1.00 for discrete analysis or difference of means negative for continuous analysis.
--: Analyses not performed due to sparse number of abnormalities.
NS or ns: Not significant ($p>0.10$).
NS* or ns*: Marginally significant ($0.05<p\leq 0.10$).
Note: P-value given if $p \leq 0.05$.
A capital "NS" denotes a relative risk 1.00 or greater for discrete analysis or difference of means nonnegative for continuous analysis; a lower case "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

Table 13-75. (Continued)
Summary of Group Analyses (Model 1) for Gastrointestinal Variables
(Ranch Hands vs. Comparisons)

	ADJUSTED			
Variable	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Medical Records				
Hepatitis (Non-A, Non-B, and Non-C) (D)	NS	NS	NS	ns
Jaundice (D)	**(ns*)	**(ns)	**(NS)	**(ns*)
Chronic Liver Disease and Cirrhosis (Alcohol-Related) (D)	ns	NS	ns	ns
Chronic Liver Disease and Cirrhosis (Nonalcohol-Related) (D)	NS	NS	NS	NS
Other Liver Disorders (D)	NS	NS	ns	NS
Hepatomegaly (D)	**(ns*)	**(ns)	**(NS)	**(-0.031)
Physical Examination				
Current Hepatomegaly (D)	ns	ns	--	ns
Laboratory				
AST (C)	ns	ns	ns*	ns
AST (D)	**(ns)	**(ns)	**(ns)	**(ns)
ALT (C)	ns*	ns	-0.026	ns
ALT (D)	**(ns)	**(NS)	**(ns)	**(ns*)
GGT (C)	NS	NS	ns	NS
GGT (D)	NS	NS	ns	NS
Alkaline Phosphatase (C)	**(+0.005)	**(NS)	**(ns)	**(+0.001)
Alkaline Phosphatase (D)	NS*	NS	ns	+0.011
Total Bilirubin (C)	ns	NS	ns	ns
Total Bilirubin (D)	NS	NS	ns	NS
Direct Bilirubin (D)	ns	NS	ns	-0.026
LDH (C)	**(NS)	**(ns)	**(ns)	**(NS*)
LDH (D)	**(NS)	**(NS)	**(NS)	**(NS)
Cholesterol (C)	**(NS)	**(NS)	**(ns)	**(NS)
Cholesterol (D)	**(NS)	**(NS)	**(NS)	**(NS)
HDL Cholesterol (C)[a]	**(ns)	**(ns)	**(NS)	**(ns)
HDL Cholesterol (D)	+0.048	+0.048	ns	NS
Cholesterol-HDL Ratio (C)	NS	NS	ns	NS
Cholesterol-HDL Ratio (D)	NS	NS	ns	NS
Triglycerides (C)	**(NS)	**(+0.039)	**(ns*)	**(NS)
Triglycerides (D)	NS	+0.050	NS	ns
Creatine Kinase (C)	**(ns)	**(NS)	**(ns)	**(ns)
Creatine Kinase (D)	**(NS)	**(NS)	**(ns)	**(ns)
Serum Amylase (C)	ns	ns*	NS	NS
Serum Amylase (D)	ns	ns	NS	NS
Antibodies for Hepatitis A (D)	ns	NS	NS	ns
Serological Evidence of Prior Hepatitis B Infection (D)	-<0.001	-0.030	ns*	ns*

Table 13-75. (Continued)
Summary of Group Analyses (Model 1) for Gastrointestinal Variables
(Ranch Hands vs. Comparisons)

Variable	ADJUSTED			
	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Antibodies for Hepatitis C (D)	**(-0.048)	**(ns)	--	**(ns)
Stool Hemoccult (D)	**(NS)	**(NS)	--	**(NS)
Prealbumin (C)[a]	**(NS)	**(NS)	**(NS)	**(ns)
Prealbumin (D)[a]	ns	ns	NS	NS
Albumin (C)	**(ns)	**(ns)	**(ns)	**(ns)
Albumin (D)	**(NS)	**(NS)	**(ns)	**(NS)
α-1 Acid Glycoprotein (C)	NS	ns	NS	NS
α-1 Acid Glycoprotein (D)	**(ns)	**(ns)	**(NS)	**(ns)
α-1 Antitrypsin (C)	NS*	NS	NS	NS
α-1 Antitrypsin (D): Low vs. Normal	NS	NS	NS	NS
α-1 Antitrypsin (C): High vs. Normal	NS	NS	NS	ns
α-2 Macroglobulin (C)	ns	ns	ns	NS
α-2 Macroglobulin (D)	ns	--	ns	NS
Apolipoprotein B (C)	ns	ns	ns	NS
Apolipoprotein B (D)	NS	NS	ns	NS
C_3 Complement (C)[a]	ns	NS	ns	ns
C_3 Complement (D)	**(NS)	**(ns)	**(ns)	**(NS)
C_4 Complement (C)[a]	ns	ns	NS	ns
C_4 Complement (D)	ns	NS	ns	NS
Haptoglobin (C)	+0.016	NS	NS	+0.034
Haptoglobin (D)	NS	NS	NS	NS
Transferrin (C)[a]	+0.040	NS	ns	+0.031
Transferrin (D)	**(ns)	**(ns)	**(NS)	**(ns)

[a] Negative difference considered adverse for this variable.

C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥ 1.00 for discrete analysis or difference of means nonnegative for continuous analysis.
-: Relative risk < 1.00 for discrete analysis or difference of means negative for continuous analysis.
--: Analysis not performed due to sparse number of abnormalities.
NS or ns: Not significant (p > 0.10).
NS* or ns*: Marginally significant (0.05<p≤0.10).
**(NS) or **(ns): Group-by-covariate interaction (p ≤ 0.05); not significant when interaction is deleted; refer to Appendix I-2 for a detailed description of this interaction.
**(NS*) or **(ns*): Group-by-covariate interaction (p≤0.05); marginally significant when interaction is deleted; refer to Appendix I-2 for a detailed description of this interaction.
**(...): Group-by-covariate interaction (p≤0.05); significant when interaction is deleted and p-value is given in parentheses; refer to Appendix I-2 for a detailed description of this interaction.
Note: A capital "NS" denotes a relative risk 1.00 or greater for discrete analysis or difference of means nonnegative for continuous analysis; a lower case "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

Table 13-76.
Summary of Initial Dioxin Analyses (Model 2) for Gastrointestinal Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
Medical Records		
Hepatitis (Non-A, Non-B, and Non-C) (D)	NS	NS
Jaundice (D)	NS	NS
Chronic Liver Disease and Cirrhosis (Alcohol-Related) (D)	NS	**(NS)
Chronic Liver Disease and Cirrhosis (Nonalcohol-Related) (D)	ns	ns
Other Liver Disorders (D)	NS	**(+0.046)
Hepatomegaly (D)	NS	NS
Physical Examination		
Current Hepatomegaly (D)	ns	ns
Laboratory		
AST (C)	NS	**(NS)
AST (D)	NS	**(ns)
ALT (C)	NS	NS
ALT (D)	NS	NS
GGT (C)	NS	**(NS)
GGT (D)	NS	NS
Alkaline Phosphatase (C)	NS	**(ns)
Alkaline Phosphatase (D)	NS	**(ns)
Total Bilirubin (C)	ns	NS
Total Bilirubin (D)	ns	**(ns)
Direct Bilirubin (D)	ns	ns
LDH (C)	NS	ns
LDH (D)	NS	NS
Cholesterol (C)	NS	**(NS*)
Cholesterol (D)	NS	**(NS)
HDL Cholesterol (C)[a]	-0.035	ns
HDL Cholesterol (D)	NS	NS
Cholesterol-HDL Ratio (C)	+0.012	**(NS)
Cholesterol-HDL Ratio (D)	NS*	NS
Triglycerides (C)	NS*	**(NS*)
Triglycerides (D)	NS	NS
Creatine Kinase (C)	NS	NS
Creatine Kinase (D)	NS	NS
Serum Amylase (C)	-0.014	-0.027
Serum Amylase (D)	ns	**(ns)
Antibodies for Hepatitis A (D)	ns	NS

Table 13-76. (Continued)
Summary of Initial Dioxin Analyses (Model 2) for Gastrointestinal Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
Serological Evidence of Prior Hepatitis B Infection (D)	NS*	NS
Antibodies for Hepatitis C (D)	ns	ns
Stool Hemoccult (D)	ns	ns
Prealbumin (C)[a]	ns	**(ns)
Prealbumin (D)	NS	NS
Albumin (C)[a]	NS	**(NS)
Albumin (D)	NS	NS
α-1 Acid Glycoprotein (C)	NS	**(ns*)
α-1 Acid Glycoprotein (D)	NS	**(NS)
α-1 Antitrypsin (C)	NS	**(NS)
α-1 Antitrypsin (D): Low vs. Normal	ns	ns
α-1 Antitrypsin (D): High vs. Normal	ns	ns
α-2 Macroglobulin (C)	ns	**(NS)
α-2 Macroglobulin (D)	NS	NS
Apolipoprotein B (C)	NS	**(+0.018)
Apolipoprotein B (D)	NS	**(NS)
C_3 Complement (C)[a]	+0.041	+0.031
C_3 Complement (D)	ns	ns
C_4 Complement (C)[a]	NS	**(NS)
C_4 Complement (D)	NS	NS
Haptoglobin (C)	NS	**(ns)
Haptoglobin (D)	NS	**(NS)
Transferrin (C)[a]	NS	**(NS)
Transferrin (D)	ns	ns

a Negative slope considered adverse for this variable.
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥ 1.00 for discrete analysis or slope nonnegative for continuous analysis.
-: Relative risk < 1.00 for discrete analysis or slope negative for continuous analysis.
NS or ns: Not significant (p>0.10).
NS*: Marginally significant (0.05<p≤0.10).
**(NS) or **(ns): Log_2 (initial dioxin)-by-covariate interaction (p≤0.05); not significant when interaction is deleted; refer to Appendix I-2 for a detailed description of this interaction.
**(NS*) or **(ns*): Log_2 (initial dioxin)-by-covariate interaction (p≤0.05); marginally significant when interaction is deleted; refer to Appendix I-2 for a detailed description of this interaction.
**(...): Log_2 (initial dioxin)-by-covariate interaction (p≤0.05); significant when interaction is deleted and p-value is given in parentheses; refer to Appendix I-2 for a detailed description of this interaction.
Note: P-value given if p ≤ 0.05.
A capital "NS" denotes a relative risk 1.00 or greater for discrete analysis or slope nonnegative for continuous analysis; a lower case "ns" denotes relative risk less than 1.00 for discrete analysis or slope negative for continuous analysis.

Table 13-77.
Summary of Categorized Dioxin Analyses (Model 3) for Gastrointestinal Variables (Ranch Hands vs. Comparisons)

	UNADJUSTED			
Variable	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Medical Records				
Hepatitis (Non-A, Non-B, or Non-C) (D)	ns	NS	ns	ns
Jaundice (D)	NS	ns*	ns*	-0.008
Chronic Liver Disease and Cirrhosis (Alcohol-Related) (D)	ns	ns	ns	ns
Chronic Liver Disease and Cirrhosis (Nonalcohol-Related) (D)	NS	NS	ns	NS
Other Liver Disorders (D)	ns	NS	NS*	NS
Hepatomegaly (D)	ns	ns*	ns	ns
Physical Examination				
Current Hepatomegaly (D)	ns	ns	NS	ns
Laboratory				
AST (C)	ns	ns	ns	ns
AST (D)	ns	NS	ns	ns
ALT (C)	-0.011	ns	NS	ns
ALT (D)	ns	ns	ns	ns
GGT (C)	ns	NS*	NS*	+0.020
GGT (D)	ns	NS	NS	NS
Alkaline Phosphatase (C)	NS	+0.002	+0.020	+0.001
Alkaline Phosphatase (D)	NS*	NS*	NS	NS*
Total Bilirubin (C)	NS	ns	-0.033	ns*
Total Bilirubin (D)	NS	ns	ns	ns
Direct Bilirubin (D)	ns	ns	ns*	ns*
LDH (C)	ns	NS	ns	ns
LDH (D)	NS	ns	ns	ns
Cholesterol (C)	ns	NS	NS	NS
Cholesterol (D)	NS	NS	NS	NS*
HDL Cholesterol (C)[a]	NS	NS	-0.017	ns
HDL Cholesterol (D)	NS*	ns	NS	NS
Cholesterol-HDL Ratio (C)	ns	ns	+0.004	NS*
Cholesterol-HDL Ratio (D)	ns	NS	+0.009	NS*
Triglycerides (C)	ns	NS	+0.008	NS*
Triglycerides (D)	NS	NS	NS*	NS
Creatine Kinase (C)	ns	ns	NS	NS
Creatine Kinase (D)	NS	ns	NS	NS
Serum Amylase (C)	ns	NS*	ns	NS
Serum Amylase (D)	ns	ns	ns	ns

Table 13-77. (Continued)
Summary of Categorized Dioxin Analyses (Model 3) for Gastrointestinal Variables (Ranch Hands vs. Comparisons)

	UNADJUSTED			
Variable	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Antibodies for Hepatitis A (D)	ns	NS	NS	NS
Serological Evidence of Prior Hepatitis B Infection (D)	-0.013	-0.030	ns	-0.033
Antibodies for Hepatitis C (D)	ns	ns	ns	ns*
Stool Hemoccult (D)	ns	+0.031	ns	NS
Prealbumin (C)[a]	ns	ns	NS	NS
Prealbumin (D)	NS	ns	ns	ns
Albumin (C)[a]	ns	ns	NS	NS
Albumin (D)	NS	NS	ns	ns
α-1 Acid Glycoprotein (C)	ns*	NS	NS	NS
α-1 Acid Glycoprotein (D)	ns	ns	ns	ns
α-1 Antitrypsin (C)	NS	NS	NS	NS
α-1 Antitrypsin (D): Low vs. Normal	NS	ns	ns	ns
α-1 Antitrypsin (D): High vs. Normal	NS	NS	ns	ns
α-2 Macroglobulin (C)	ns	ns	ns	ns
α-2 Macroglobulin (D)	ns	--	NS	ns
Apolipoprotein B (C)	ns	ns	NS	NS
Apolipoprotein B (D)	ns	NS	NS*	NS
C_3 Complement (C)[a]	-0.004	NS	NS*	NS*
C_3 Complement (D)	NS	ns	ns	ns
C_4 Complement (C)[a]	ns	NS	ns	NS
C_4 Complement (D)	NS	ns	ns	ns
Haptoglobin (C)	NS	NS	+0.003	+0.007
Haptoglobin (D)	NS	NS	NS*	NS
Transferrin (C)[a]	ns	+0.044	+0.001	+0.001
Transferrin (D)	ns	ns*	-0.015	-0.005

[a]Negative difference considered adverse for this variable.
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥ 1.00 for discrete analysis or difference of means nonnegative for continuous analysis.
-: Relative risk < 1.00 for discrete analysis or difference of means negative for continuous analysis.
--: Analysis not performed due to sparse number of abnormalities.
NS or ns: Not significant (p>0.10).
NS* or ns*: Marginally significant (0.05 <p ≤ 0.10).
Note: P-value given if p ≤ 0.05.
A capital "NS" denotes a relative risk 1.00 or greater for discrete analysis or difference of means nonnegative for continuous analysis; a lower case "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

Table 13-77. (Continued)
Summary of Categorized Dioxin Analyses (Model 3) for Gastrointestinal Variables (Ranch Hands vs. Comparisons)

	ADJUSTED			
Variable	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Medical Records				
Hepatitis (Non-A, Non-B, Non-C) (D)	NS	NS	ns	ns
Jaundice (D)	NS	-0.046	ns	-0.011
Chronic Liver Disease and Cirrhosis (Alcohol-Related) (D)	**(ns)	**(ns)	**(ns)	**(ns)
Chronic Liver Disease and Cirrhosis (Nonalcohol-Related) (D)	NS	NS	ns	ns
Other Liver Disorders (D)	**(ns)	**(NS)	**(+0.048)	**(NS)
Hepatomegaly (D)	ns	ns*	NS	ns
Physical Examination				
Current Hepatomegaly (D)	ns	ns	NS	ns
Laboratory				
AST (C)	ns	ns	ns	ns
AST (D)	**(ns)	**(NS)	**(ns)	**(ns)
ALT (C)	ns*	ns	ns	ns
ALT (D)	**(ns)	**(ns)	**(ns)	**(ns)
GGT (C)	**(ns)	**(NS*)	**(+0.031)	**(+0.011)
GGT (D)	**(ns)	**(NS)	**(NS)	**(NS*)
Alkaline Phosphatase (C)	**(+0.043)	**(+0.006)	**(NS)	**(+0.011)
Alkaline Phosphatase (D)	+0.030	NS*	NS	NS
Total Bilirubin (C)	NS	ns	ns	ns
Total Bilirubin (D)	NS	ns	ns	ns
Direct Bilirubin (D)	ns	ns	ns	ns
LDH (C)	**(NS)	**(ns)	**(ns)	**(ns)
LDH (D)	**(NS)	**(ns)	**(NS)	**(ns)
Cholesterol (C)	**(NS)	**(ns)	**(NS)	**(NS)
Cholesterol (D)	**(NS)	**(NS)	**(NS)	**(NS)
HDL Cholesterol (C)[a]	**(NS)	**(NS)	**(ns)	**(ns)
HDL Cholesterol (D)	**(NS)	**(NS)	**(NS)	**(NS)

Table 13-77. (Continued)
Summary of Categorized Dioxin Analyses (Model 3) for Gastrointestinal Variables (Ranch Hands vs. Comparisons)

	ADJUSTED			
Variable	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Cholesterol-HDL Ratio (C)	**(ns)	**(ns)	**(NS)	**(NS)
Cholesterol-HDL Ratio (D)	NS	NS	NS	NS
Triglycerides (C)	ns	NS	+0.031	NS
Triglycerides (D)	ns	NS	+0.036	NS
Creatine Kinase (C)	**(ns)	**(ns)	**(NS)	**(ns)
Creatine Kinase (D)	**(NS)	**(ns)	**(NS)	**(NS)
Serum Amylase (C)	ns	NS	ns	NS
Serum Amylase (D)	**(ns)	**(ns)	**(ns)	**(ns)
Antibodies for Hepatitis A (D)	NS	ns	ns	ns
Serological Evidence of Prior Hepatitis B Infection (D)	**(ns)	**(-0.020)	**(-0.041)	**(-0.004)
Antibodies for Hepatitis C (D)	ns	ns	ns	-0.048
Stool Hemoccult (D)	ns	+0.037	NS	NS
Prealbumin (C)[a]	**(ns)	**(NS)	**(NS)	**(NS)
Prealbumin (D)	NS	ns	ns	ns
Albumin (C)[a]	**(ns)	**(ns)	**(NS)	**(NS)
Albumin (D)	NS	NS	ns	ns
α-1 Acid Glycoprotein (C)	**(ns)	**(NS)	**(NS)	**(NS)
α-1 Acid Glycoprotein (D)	**(ns)	**(ns)	**(NS)	**(ns)
α-1 Antitrypsin (C)	+0.010	NS	ns	NS
α-1 Antitrypsin (D): Low vs. Normal	NS	ns	NS	NS
α-1 Antitrypsin (D): High vs. Normal	NS	NS	ns	ns
α-2 Macroglobulin (C)	NS	ns	ns	ns*
α-2 Macroglobulin (D)	ns	--	NS	ns
Apolipoprotein B (C)	ns	ns	NS	NS
Apolipoprotein B (D)	NS	ns	NS	NS
C_3 Complement (C)[a]	-0.043	NS	NS	NS
C_3 Complement (D)	**(NS)	**(ns)	**(ns)	**(ns)
C_4 Complement (C)[a]	ns	NS	ns	ns
C_4 Complement (D)	ns	ns	ns	ns

Table 13-77. (Continued)
Summary of Categorized Dioxin Analyses (Model 3) for Gastrointestinal Variables (Ranch Hands vs. Comparisons)

	ADJUSTED			
Variable	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Haptoglobin (C)	NS*	NS	NS*	NS
Haptoglobin (D)	NS	ns	NS	NS
Transferrin (C)[a]	NS	+0.035	+0.003	+0.001
Transferrin (D)	**(ns)	**(ns*)	**(-0.042)	**(-0.009)

[a] Negative difference considered adverse for this variable.
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk $\geq$ 1.00 for discrete analysis or difference of means nonnegative for continuous analysis.
-: Relative risk $<$ 1.00 for discrete analysis or difference of means negative for continuous analysis.
--: Analysis not performed due to sparse number of abnormalities.
NS or ns: Not significant ($p>0.10$).
NS* or ns*: Marginally significant ($0.05<p\leq 0.10$).
**(NS) or **(ns): Categorized dioxin-by-covariate interaction ($p\leq 0.05$); not significant when interaction is deleted; refer to Appendix I-2 for a detailed description of this interaction.
**(NS*) or **(ns*): Categorized dioxin-by-covariate interaction ($p\leq 0.05$); marginally significant when interaction is deleted; refer to Appendix I-2 for a detailed description of this interaction.
**(...): Categorized dioxin-by-covariate interaction ($p\leq 0.05$); significant when interaction is deleted and p-value is given in parentheses; refer to Appendix I-2 for a detailed description of this interaction.
Note: P-value given if $p\leq 0.05$.
A capital "NS" denotes a relative risk 1.00 or greater for discrete analysis or difference of means nonnegative for continuous analysis; a lower case "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

Table 13-78.
Summary of Current Dioxin Analyses (Models 4, 5, and 6) for Gastrointestinal Variables (Ranch Hands Only)

Variable	UNADJUSTED		
	Model 4: Lipid-Adjusted Current Dioxin	Model 5: Whole-Weight Current Dioxin	Model 6: Whole-Weight Current Dioxin Adjusted for Total Lipids
Medical Records			
Hepatitis (Non-A, Non-B, or Non-C) (D)	NS	ns	NS
Jaundice (D)	-<0.001	-<0.001	-<0.001
Chronic Liver Disease and Cirrhosis (Alcohol-Related) (D)	NS	NS	NS
Chronic Liver Disease and Cirrhosis (Nonalcohol-Related) (D)	NS	NS	NS
Other Liver Disorders (D)	+0.007	+0.003	+0.033
Hepatomegaly (D)	NS	ns	ns
Physical Examination			
Current Hepatomegaly (D)	NS	NS	NS
Laboratory			
AST (C)	NS	NS*	NS
AST (D)	NS	NS	NS
ALT (C)	+<0.001	+<0.001	+<0.001
ALT (D)	+0.031	+0.017	NS*
GGT (C)	+<0.001	+<0.001	+0.002
GGT (D)	+0.033	+0.009	NS
Alkaline Phosphatase (C)	NS	NS	NS
Alkaline Phosphatase (D)	NS	NS	ns
Total Bilirubin (C)	ns	ns	ns
Total Bilirubin (D)	ns	ns	ns
Direct Bilirubin (D)	ns	NS	ns*
LDH (C)	NS	NS	NS
LDH (D)	NS	NS	NS
Cholesterol (C)	NS	+<0.001	ns*
Cholesterol (D)	NS	+0.003	ns
HDL Cholesterol (C)[a]	-<0.001	-<0.001	-0.001
HDL Cholesterol (D)	NS	NS	ns
Cholesterol-HDL Ratio (C)	+<0.001	+<0.001	+0.035
Cholesterol-HDL Ratio (D)	+<0.001	+<0.001	NS
Triglycerides (C)	+<0.001	+<0.001	+0.041
Triglycerides (D)	+0.013	+<0.001	NS
Creatine Kinase (C)	+0.017	+0.011	+0.027
Creatine Kinase (D)	NS	NS	NS
Serum Amylase (C)	-0.037	-0.019	ns
Serum Amylase (D)	ns	ns	ns
Antibodies for Hepatitis A (D)	NS	NS	NS

Table 13-78. (Continued)
Summary of Current Dioxin Analyses (Models 4, 5, and 6) for Gastrointestinal Variables (Ranch Hands Only)

	UNADJUSTED		
Variable	Model 4: Lipid-Adjusted Current Dioxin	Model 5: Whole-Weight Current Dioxin	Model 6: Whole-Weight Current Dioxin Adjusted for Total Lipids
Serological Evidence of Prior Hepatitis B Infection (D)	NS*	NS	NS
Antibodies for Hepatitis C (D)	ns	ns	ns
Stool Hemoccult (D)	NS	NS	NS
Prealbumin (C)[a]	ns	NS	ns
Prealbumin (D)	ns	ns	ns
Albumin (C)[a]	NS	NS	NS
Albumin (D)	NS	NS	NS
α-1 Acid Glycoprotein (C)	NS*	+0.015	NS
α-1 Acid Glycoprotein (D)	NS	NS	NS
α-1 Antitrypsin (C)	ns	ns	ns
α-1 Antitrypsin (D) Low vs. Normal	ns	ns	ns
α-1 Antitrypsin (D) High vs. Low	ns*	ns*	ns
α-2 Macroglobulin (C)	-0.029	-0.046	-0.018
α-2 Macroglobulin (D)	NS	NS	NS
Apolipoprotein B (C)	+0.016	+<0.001	ns
Apolipoprotein B (D)	NS*	+0.001	ns
C_3 Complement (C)[a]	+<0.001	+<0.001	+<0.001
C_3 Complement (D)	-0.014	-0.003	ns
C_4 Complement (C)[a]	NS*	+0.004	NS
C_4 Complement (D)	ns	ns	ns
Haptoglobin (C)	NS	NS	NS
Haptoglobin (D)	ns	NS	ns
Transferrin (C)[a]	+0.001	+<0.001	+0.009
Transferrin (D)	-0.049	ns*	-0.048

[a]Negative slope considered adverse for this variable.
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥ 1.00 for discrete analysis or slope nonnegative for continuous analysis.
-: Relative risk < 1.00 for discrete analysis or slope negative for continuous analysis.
NS or ns: Not significant (p>0.10).
NS* or ns*: Marginally significant (0.05<p≤0.10).
Note: P-value given if p≤0.05.
A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or slope nonnegative for continuous analysis; a lower case "ns" denotes relative risk less than 1.00 for discrete analysis or slope negative for continuous analysis.

Table 13-78. (Continued)
Summary of Current Dioxin Analyses (Models 4, 5, and 6) for Gastrointestinal Variables (Ranch Hands Only)

Variable	ADJUSTED		
	Model 4: Lipid-Adjusted Current Dioxin	Model 5: Whole-Weight Current Dioxin	Model 6: Whole-Weight Current Dioxin Adjusted for Total Lipids
Medical Records			
Hepatitis (Non-A, Non-B, or Non-C) (D)	ns	ns	ns
Jaundice (D)	-<0.001	-<0.001	-<0.001
Chronic Liver Disease and Cirrhosis (Alcohol-Related) (D)	NS	NS	NS
Chronic Liver Disease and Cirrhosis (Nonalcohol-Related) (D)	NS	NS	NS
Other Liver Disorders (D)	**(+0.004)	**(+0.001)	**(+0.018)
Hepatomegaly (D)	ns	ns	ns
Physical Examination			
Current Hepatomegaly (D)	NS	NS	NS
Laboratory			
AST (C)	**(NS)	**(NS*)	**(NS)
AST (D)	**(NS)	**(NS)	**(NS)
ALT (C)	+<0.001	+<0.001	+<0.001
ALT (D)	+0.035	+0.024	NS*
GGT (C)	**(+<0.001)	**(+<0.001)	**(+0.002)
GGT (D)	**(+0.040)	**(+0.012)	**(NS)
Alkaline Phosphatase (C)	**(ns)	**(ns)	**(ns*)
Alkaline Phosphatase (D)	ns	ns	ns
Total Bilirubin (C)	**(NS)	NS	NS
Total Bilirubin (D)	**(ns)	**(ns)	**(ns)
Direct Bilirubin (D)	**(NS)	**(NS)	**(ns)
LDH (C)	NS	NS	NS
LDH (D)	NS	NS	NS
Cholesterol (C)	NS	+<0.001	ns
Cholesterol (D)	NS	**(+0.002)	ns
HDL Cholesterol (C)[a]	**(-0.001)	**(-<0.001)	**(-0.022)
HDL Cholesterol (D)	**(NS)	**(NS*)	**(NS)
Cholesterol-HDL Ratio (C)	**(+<0.001)	**(+<0.001)	**(NS*)
Cholesterol-HDL Ratio (D)	+0.006	+<0.001	NS
Triglycerides (C)	**(+<0.001)	**(+<0.001)	**(+0.007)
Triglycerides (D)	+0.002	+<0.001	NS
Creatine Kinase (C)	+0.003	+0.002	+0.006
Creatine Kinase (D)	NS*	NS*	NS*
Serum Amylase (C)	-0.010	-0.005	ns*
Serum Amylase (D)	ns	ns	ns
Antibodies for Hepatitis A (D)	NS	NS	NS

Table 13-78. (Continued)
Summary of Current Dioxin Analyses (Models 4, 5, and 6) for Gastrointestinal Variables (Ranch Hands Only)

Variable	ADJUSTED		
	Model 4: Lipid-Adjusted Current Dioxin	Model 5: Whole-Weight Current Dioxin	Model 6: Whole-Weight Current Dioxin Adjusted for Total Lipids
Serological Evidence of Prior Hepatitis B Infection (D)	**(ns)	**(ns)	**(ns)
Antibodies for Hepatitis C (D)	ns	ns	ns
Stool Hemoccult (D)	NS	NS	NS
Prealbumin (C)[a]	**(ns)	**(NS)	**(ns)
Prealbumin (D)	**(ns)	**(ns)	**(NS)
Albumin (C)[a]	**(ns)	**(NS)	**(ns)
Albumin (D)	NS	NS	NS
α-1 Acid Glycoprotein (C)	**(ns*)	ns	-0.040
α-1 Acid Glycoprotein (D)	**(ns)	**(ns)	**(NS)
α-1 Antitrypsin (C)	**(-0.004)	**(-<0.001)	**(-0.007)
α-1 Antitrypsin (D): Low vs. Normal	ns	ns	ns
α-1 Antitrypsin (D): High vs. Normal	ns*	-0.035	ns
α-2 Macroglobulin (C)	-0.006	-0.008	-0.007
α-2 Macroglobulin (D)	NS	NS	NS
Apolipoprotein B (C)	+0.026	**(+<0.001)	ns
Apolipoprotein B (D)	NS*	**(+<0.001)	ns
C_3 Complement (C)[a]	+<0.001	**(+<0.001)	+<0.001
C_3 Complement (D)	**(-0.032)	-0.003	ns
C_4 Complement (C)[a]	NS	**(+0.018)	NS
C_4 Complement (D)	ns	ns	ns
Haptoglobin (C)	ns	ns	ns
Haptoglobin (D)	ns	ns	-0.044
Transferrin (C)[a]	+0.012	+0.001	+0.040
Transferrin (D)	-0.043	-0.041	-0.039

[a]Negative slope considered adverse for this variable.
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥ 1.00 for discrete analysis or slope nonnegative for continuous analysis.
-: Relative risk < 1.00 for discrete analysis or slope negative for continuous analysis.
NS or ns: Not significant ($p>0.10$).
NS* or ns*: Marginally significant ($0.05<p\leq 0.10$).
**(NS) or **(ns): Log_2 (current dioxin + 1)-by-covariate interaction ($p\leq 0.05$); not significant when interaction is deleted; refer to Appendix I-2 for a detailed description of this interaction.
**(NS*) or **(ns*): Log_2 (current dioxin + 1)-by-covariate interaction ($0.01<p\leq 0.05$); marginally significant when interaction is deleted; refer to Appendix I-2 for a detailed description of this interaction.
**(...): Log_2 (current dioxin + 1)-by-covariate interaction ($0.01<p\leq 0.05$); significant when interaction is deleted and p-value given in parentheses; refer to Appendix I-2 for a detailed description of this interaction.
Note: P-value given if $p\leq 0.05$.
A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or a nonnegative slope for continuous analysis; a lower case "ns" denotes relative risk less than 1.00 for discrete analysis or slope negative for continuous analysis.

Table 13-79.
Summary of Group-by-Covariate and Dioxin-by-Covariate Interactions from Adjusted Analyses of Gastrointestinal Variables

Model	Variable	Covariate
1[a]	Jaundice (D)	Race
	Hepatomegaly (D)	Occupation
	AST (D)	Current Alcohol Use
	ALT (D)	Age
		Degreasing Chemical Exposure
	Alkaline Phosphatase (C)	Age
		Race
		Degreasing Chemical Exposure
	LDH (C)	Age
		Lifetime Alcohol History
	LDH (D)	Current Alcohol Use
	Cholesterol (C)	Current Alcohol Use
	Cholesterol (D)	Current Alcohol Use
	HDL Cholesterol (C)	Current Alcohol Use
		Lifetime Alcohol History
	Triglycerides (C)	Occupation
	Creatine Kinase (C)	Race
	Creatine Kinase (D)	Race
	Antibodies for Hepatitis C	Age
		Degreasing Chemical Exposure
	Stool Hemoccult (D)	Lifetime Alcohol History
	Prealbumin (C)	Current Alcohol Use
	Albumin (C)	Lifetime Alcohol History
		Age
	Albumin (D)	Industrial Chemical Exposure
	α-1 Acid Glycoprotein (D)	Age
	C_3 Complement (D)	Race
	Transferrin (D)	Lifetime Alcohol History

Table 13-79. (Continued)
Summary of Group-by-Covariate and Dioxin-by-Covariate Interactions from Adjusted Analyses of Gastrointestinal Variables

Model	Variable	Covariate
2[b]	Alcoholic Chronic Liver Disease and Cirrhosis (D)	Race
	Other Liver Disorders (D)	Occupation
	AST (C)	Current Alcohol Use
	AST (D)	Current Alcohol Use
	GGT (C)	Degreasing Chemical Exposure
	Alkaline Phosphatase (C)	Degreasing Chemical Exposure
	Alkaline Phosphatase (D)	Industrial Chemical Exposure
	Total Bilirubin (D)	Industrial Chemical Exposure
	Cholesterol (C)	Degreasing Chemical Exposure
	Cholesterol (D)	Degreasing Chemical Exposure Lifetime Alcohol History
	Cholesterol-HDL Ratio (C)	Current Alcohol Use
	Triglycerides (C)	Occupation
	Serum Amylase (D)	Age
	Prealbumin (C)	Industrial Chemical Exposure
	Albumin (C)	Industrial Chemical Exposure
	α-1 Acid Glycoprotein (C)	Lifetime Alcohol History Occupation
	α-1 Acid Glycoprotein (D)	Occupation Degreasing Chemical Exposure
	α-1 Antitrypsin (C)	Industrial Chemical Exposure Degreasing Chemical Exposure
	α-2 Macroglobulin (C)	Age
	Apolipoprotein B (C)	Age
	Apolipoprotein B (D)	Age
	C_4 Complement (C)	Occupation Age
	Haptoglobin (C)	Age Lifetime Alcohol History
	Haptoglobin (D)	Occupation Lifetime Alcohol History
	Transferrin (C)	Occupation Industrial Chemical Exposure

Table 13-79. (Continued)
Summary of Group-by-Covariate and Dioxin-by-Covariate Interactions from Adjusted Analyses of Gastrointestinal Variables

Model	Variable	Covariate
3[c]	Alcoholic Chronic Liver Disease and Cirrhosis (D)	Race
	Other Liver Disorders (D)	Degreasing Chemical Exposure
	AST (D)	Current Alcohol Use
	ALT (D)	Degreasing Chemical Exposure
		Current Alcohol Use
	GGT (C)	Degreasing Chemical Exposure
	GGT (D)	Degreasing Chemical Exposure
	Alkaline Phosphatase (C)	Degreasing Chemical Exposure
	LDH (C)	Age
		Race
		Lifetime Alcohol History
	LDH (D)	Lifetime Alcohol History
	Cholesterol (C)	Lifetime Alcohol History
	Cholesterol (D)	Current Alcohol Use
	HDL Cholesterol (C)	Current Alcohol Use
		Lifetime Alcohol History
	HDL Cholesterol (D)	Lifetime Alcohol History
	Cholesterol-HDL Ratio (C)	Current Alcohol Use
	Creatine Kinase (C)	Race
		Lifetime Alcohol History
	Creatine Kinase (D)	Race
		Lifetime Alcohol History
	Serum Amylase (D)	Race
	Serological Evidence of Prior Hepatitis B Infection (D)	Occupation
		Age
	Prealbumin (C)	Industrial Chemical Exposure
	Albumin (C)	Industrial Chemical Exposure
	α-1 Acid Glycoprotein (C)	Lifetime Alcohol History
	α-1 Acid Glycoprotein (D)	Age
	C_3 Complement (D)	Race
		Industrial Chemical Exposure
	Transferrin (D)	Lifetime Alcohol History

Table 13-79. (Continued)
Summary of Group-by-Covariate and Dioxin-by-Covariate Interactions from Adjusted Analyses of Gastrointestinal Variables

Model	Variable	Covariate
4[d]	Other Liver Disorders (D)	Occupation
		Degreasing Chemical Exposure
	AST (C)	Current Alcohol Use
	AST (D)	Current Alcohol Use
	GGT (C)	Occupation
	GGT (D)	Degreasing Chemical Exposure
	Alkaline Phosphatase (C)	Race
	Total Bilirubin (C)	Degreasing Chemical Exposure
	Total Bilirubin (D)	Degreasing Chemical Exposure
	Direct Bilirubin (D)	Lifetime Alcohol History
	HDL Cholesterol (C)	Lifetime Alcohol History
		Current Alcohol Use
	HDL Cholesterol (D)	Lifetime Alcohol History
	Cholesterol-HDL Ratio (C)	Degreasing Chemical Exposure
	Triglycerides (C)	Occupation
	Serological Evidence of Prior Hepatitis B Infection (D)	Occupation
	Prealbumin (C)	Degreasing Chemical Exposure
		Industrial Chemical Exposure
	Prealbumin (D)	Occupation
	Albumin (C)	Current Alcohol Use
		Degreasing Chemical Exposure
	α-1 Acid Glycoprotein (C)	Lifetime Alcohol History
	α-1 Acid Glycoprotein (D)	Occupation
	α-1 Antitrypsin (C)	Occupation
		Degreasing Chemical Exposure
	C_3 Complement (D)	Current Alcohol Use

Table 13-79. (Continued)
Summary of Group-by-Covariate and Dioxin-by-Covariate Interactions from Adjusted Analyses of Gastrointestinal Variables

Model	Variable	Covariate
5[e]	Other Liver Disorders (D)	Occupation
		Degreasing Chemical Exposure
	AST (C)	Current Alcohol Use
	AST (D)	Current Alcohol Use
	GGT (C)	Occupation
	GGT (D)	Degreasing Chemical Exposure
	Alkaline Phosphatase (C)	Race
	Total Bilirubin (D)	Degreasing Chemical Exposure
	Direct Bilirubin (D)	Lifetime Alcohol History
	Cholesterol (D)	Occupation
	HDL Cholesterol (C)	Lifetime Alcohol History
		Current Alcohol Use
	HDL Cholesterol (D)	Lifetime Alcohol History
	Cholesterol-HDL Ratio (C)	Age
	Triglycerides (C)	Occupation
		Lifetime Alcohol History
	Serological Evidence of Prior Hepatitis B Infection (D)	Occupation
	Prealbumin (C)	Degreasing Chemical Exposure
		Occupation
	Prealbumin (D)	Occupation
	Albumin (C)	Current Alcohol Use
		Degreasing Chemical Exposure
	α-1 Acid Glycoprotein (D)	Occupation
	α-1 Antitrypsin (C)	Occupation
		Degreasing Chemical Exposure
	Apolipoprotein B (C)	Age
	Apolipoprotein B (D)	Age
	C_3 Complement (C)	Occupation
	C_4 Complement (C)	Occupation

Table 13-79. (Continued)
Summary of Group-by-Covariate and Dioxin-by-Covariate Interactions from Adjusted Analyses of Gastrointestinal Variables

Model	Variable	Covariate
6[f]	Other Liver Disorders (D)	Occupation
		Degreasing Chemical Exposure
	AST (C)	Current Alcohol Use
	AST (D)	Current Alcohol Use
	GGT (C)	Occupation
	GGT (D)	Degreasing Chemical Exposure
	Alkaline Phosphatase (C)	Race
	Total Bilirubin (D)	Degreasing Chemical Exposure
	Direct Bilirubin (D)	Lifetime Alcohol History
	HDL Cholesterol (C)	Lifetime Alcohol History
		Current Alcohol Use
		Degreasing Chemical Exposure
	HDL Cholesterol (D)	Lifetime Alcohol History
	Cholesterol-HDL Ratio (C)	Degreasing Chemical Exposure
	Triglycerides (C)	Occupation
		Lifetime Alcohol History
	Serological Evidence of Prior Hepatitis B Infection (D)	Occupation
	Prealbumin (C)	Degreasing Chemical Exposure
		Industrial Chemical Exposure
	Prealbumin (D)	Age
	Albumin (C)	Current Alcohol Use
		Degreasing Chemical Exposure
	α-1 Acid Glycoprotein (D)	Occupation
	α-1 Antitrypsin (C)	Occupation
		Degreasing Chemical Exposure

C: Continuous analysis.
D: Discrete analysis.

[a] Group Analysis (Ranch Hands vs. Comparison).
[b] Ranch Hands—Log_2 (Initial Dioxin).
[c] Categorized Dioxin.
[d] Ranch Hands—Log_2 (Current Lipid-Adjusted Dioxin + 1).
[e] Ranch Hands—Log_2 (Current Whole-Weight Dioxin + 1).
[f] Ranch Hands—Log_2 (Current Whole-Weight Dioxin + 1), Adjusted for Total Lipids.

Medical Records

Historical information collected at the 1982, 1985, and 1987 examinations was updated with data collected at the 1992 health interview and grouped by ICD code into eight categories of liver disorders for analysis: hepatitis (non-A, non-B, and non-C), jaundice, acute and subacute necrosis of the liver, chronic liver disease and cirrhosis (alcohol-related), chronic liver disease and cirrhosis (nonalcohol-related), liver abscess and sequelae of chronic liver disease, other liver disorders, and hepatomegaly. All conditions were verified through medical records.

Model 1: Group Analysis

The unadjusted overall group contrasts found no significant differences between the Ranch Hands and the Comparisons for any of the liver disorder variables. After covariate adjustment, the overall group difference became marginally significant for jaundice (Adj. RR=0.62, p=0.100) and for hepatomegaly (Adj. RR=0.61, p=0.100) with relatively fewer Ranch Hands than Comparisons having a history of both of these conditions. The adjusted analyses for the other historical liver conditions were not significant.

The results of the occupation-stratified analyses were similar to the overall contrast findings. The unadjusted analyses of jaundice and hepatomegaly found marginally significant relative risks less than one for Ranch Hands in the enlisted groundcrew stratum. After covariate adjustment, the relative risk remained marginally less than one for jaundice and became significantly less than one for hepatomegaly. The unadjusted and adjusted results within the officer stratum and within the enlisted flyer stratum were not significant for any of the historical liver disorder variables.

Model 2: Initial Dioxin Analysis

The unadjusted Model 2 analyses did not show a significant association between estimated initial dioxin exposure and any of the historical liver disorders. After adjusting for occupation, the analyses of the category of other liver disorders revealed a significant positive association with initial dioxin. This variable is a composite of elevations from numerous laboratory tests performed during previous AFHS examinations, does not represent any specific disease or condition, and is not clinically or epidemiologically relevant. The adjusted analyses were not significant for any of the other questionnaire variables.

Model 3: Categorized Dioxin Analysis

The unadjusted and adjusted Model 3 categorized dioxin analyses found significant or marginally significant Ranch Hand dioxin category versus Comparison group contrasts for jaundice, other liver disorders, and hepatomegaly. No significant results were seen for the other variables.

The adjusted analyses of jaundice found a relative risk significantly less than one for Ranch Hands in the low dioxin category. The adjusted relative risk was less than one, but not significant for Ranch Hands in the high dioxin category. Combining the low and high

dioxin categories together led to a relative risk significantly less than one (Adj. RR=0.21, 95% C.I.=[0.06, 0.70]. p=0.011).

The adjusted analyses of hepatomegaly found that the relative risk was marginally less than one for low Ranch Hands, but the relative risk was not significant for the other contrasts. The adjusted relative risk for the composite variable of other liver disorders was significantly greater than one for Ranch Hands in the high dioxin category (Adj. RR=1.37, 95% C.I.=[1.00, 1.86], p=0.048).

Models 4 through 6: Current Dioxin Analysis

The unadjusted and adjusted analyses for Models 4, 5, and 6 found highly significant inverse relationships between current dioxin levels and a history of jaundice ($p<0.001$ in all analyses). By contrast, the analyses found strong positive associations between current dioxin levels and the composite category of other liver disorders (p=0.004, p=0.001, and p=0.018 in the adjusted Model 4, 5, and 6 analyses). Current dioxin levels were not significantly associated with any of the other historical conditions.

Physical Examination Variable

There were no significant findings in the Models 1 through 6 analyses of hepatomegaly diagnosed at the 1992 examination.

Laboratory Variables

The gastrointestinal assessment analyzed 27 laboratory variables including hepatic enzymes; bilirubin measures, lipid and carbohydrate indices, serological markers for hepatitis (A, B, and C), stool hemoccult, and 10 protein profile components. Twenty-two variables were analyzed in both continuous and discrete forms. Five were analyzed as discrete variables only.

Model 1: Group Analysis

Overall, the Model 1 assessment of group contrasts for the laboratory variables did not reveal a consistent pattern of significant group differences that would indicate that the gastrointestinal health of the Ranch Hands differs substantially from the Comparisons. Isolated significant and marginally significant findings are highlighted below.

The adjusted Model 1 analyses of the continuous variables found that the Ranch Hand group had significantly or marginally significantly higher mean levels of alkaline phosphatase, α-1 antitrypsin, haptoglobin, and transferrin, and a marginally lower mean ALT. In the discrete analyses, the relative risk was significantly more than one for abnormal low HDL levels and marginally more than one for abnormal high alkaline phosphatase levels. The elevated alkaline phosphatase findings also have been noted at previous examinations. Ranch Hands also had significantly lower serological evidence of prior hepatitis B infection and hepatitis C antibodies than Comparisons, possibly related to the longer amount of time Comparisons generally spent in SEA (see Chapter 8, Covariate Associations with Estimates

of Dioxin Exposure), with its endemic levels of hepatitis. The only consistent finding among the three occupational cohorts was a significant or marginally significant decreased prevalence of serological evidence of prior hepatitis B infection for Ranch Hands. Other significant findings were that Ranch Hand officers had more abnormal low HDL cholesterol and abnormal high triglycerides levels, and a marginally lower mean serum amylase than did Comparison officers. Ranch Hand enlisted flyers had significantly or marginally lower mean levels of AST, ALT, and triglycerides than did Comparison enlisted flyers.

The adjusted analyses of the continuous variables found that Ranch Hand group mean levels of alkaline phosphatase, LDH, haptoglobin, and transferrin were significantly higher or marginally higher than the corresponding Comparison group means in the enlisted groundcrew stratum. The adjusted discrete analyses found significantly more abnormal high alkaline phosphatase levels, significantly fewer abnormal high direct bilirubin levels, and marginally fewer abnormal high ALT levels in Ranch Hand enlisted groundcrew compared to Comparison enlisted groundcrew.

Model 2: Initial Dioxin Analysis

The adjusted Model 2 analyses detected several significant or marginally significant associations between the laboratory variables and estimated initial dioxin levels in Ranch Hands, but no consistent overall pattern was noted.

The discrete analyses detected no significant associations. In the continuous analyses, significant or marginally significant increasing associations were found for cholesterol, triglycerides, apolipoprotein B, and C_3 complement. A significant decreasing association was found with serum amylase and a marginally significant decreasing association was found with α-1 acid glycoprotein. The unadjusted analyses of HDL cholesterol and the cholesterol-HDL ratio were significant, but the relationship became nonsignificant after adjusting for occupation.

Model 3: Categorized Dioxin Analysis

The adjusted results of the high Ranch Hand versus Comparison contrast found that Ranch Hands had significantly higher mean levels of GGT, triglycerides, and transferrin, and a marginally higher mean level of haptoglobin. The discrete analyses for triglycerides and transferrin also were significant, with Ranch Hands in the high dioxin category having a higher prevalence of abnormal high triglyceride levels and a lower prevalence of abnormal low transferrin levels. In addition, the relative risk of serological evidence of prior hepatitis B infection was significantly less than one for Ranch Hands in the high initial dioxin category.

The adjusted results of the low Ranch Hand versus Comparison contrast found that Ranch Hands had a marginally higher mean GGT, a significantly higher mean level and a relative risk marginally greater than one for alkaline phosphatase, and a significantly higher mean level and a relative risk marginally less than one for transferrin. The analyses also found that Ranch Hands in the low dioxin category had a relative risk significantly greater than one for the presence of blood in their stools. As with the high versus Comparison

contrast, the relative risk of serological evidence of prior hepatitis B infection was significantly less than one for Ranch Hands in the low dioxin category.

The analyses of the low plus high Ranch Hand category versus the Comparison group found several significant or marginally significant differences. In the adjusted analyses, Ranch Hands had significantly higher mean levels of GGT and alkaline phosphatase, and marginally higher prevalence of GGT abnormal levels than did Comparisons. The unadjusted analyses for the lipid and carbohydrate indices found that Ranch Hands had marginally more cholesterol abnormalities, a marginally higher mean and more abnormalities for the cholesterol-HDL ratio, and a marginally higher mean triglycerides level, but these differences became nonsignificant after the model was adjusted for occupation.

For the serological hepatitis markers, Ranch Hands in the low plus high dioxin category had significantly lower evidence of present or prior hepatitis B infection and antibodies for hepatitis C. The adjusted analyses of the protein profile variables found a marginally lower mean level of α-2 macroglobulin, a significantly higher mean level of transferrin, and a significantly lower prevalence of abnormal low transferrin levels for Ranch Hands in the low plus high category relative to the Comparison group.

The adjusted analyses also detected several significant differences for the background Ranch Hands versus the Comparison group contrast, mostly in the analyses of the continuous variables. The only statistically significant finding in the discrete analyses was that background Ranch Hands had more abnormal high alkaline phosphatase levels than the Comparison group. In the continuous analyses, background Ranch Hands had significantly or marginally higher mean levels of alkaline phosphatase, α-1 antitrypsin, and haptoglobin, and significantly or marginally lower mean levels of ALT and C_3 complement.

Models 4 through 6: Current Dioxin Analysis

The results of the Model 4 through 6 analyses found many highly significant associations between the laboratory variables and current dioxin levels, both lipid-adjusted and whole-weight. For the hepatic enzymes ALT and GGT, there was a strong positive association with lipid-adjusted and whole-weight dioxin in both the continuous and discrete analyses. The results for AST were not significant except for a marginally significant increasing association with whole-weight dioxin in the Model 5 continuous analysis.

For the lipid and carbohydrate indices, the adjusted current dioxin analyses detected highly significant positive associations with cholesterol, the cholesterol-HDL ratio and triglycerides, as well as highly significant decreasing associations with HDL cholesterol in at least one of the models. The Model 5 whole-weight dioxin results for cholesterol, HDL cholesterol, cholesterol-HDL ratio, and triglycerides were nearly all highly significant in both the discrete and continuous analyses ($p<0.01$ for all analyses except HDL cholesterol analyzed in its discrete form, which was marginally significant). The Model 4 lipid-adjusted dioxin analyses were not significant for cholesterol, but were highly significant for HDL cholesterol (continuous only), the cholesterol-HDL ratio (continuous and discrete) and triglycerides (continuous and discrete). The Model 6 results, which used serum lipid levels as an adjusting covariate, were not significant for cholesterol, but were significant for HDL

cholesterol (continuous only), marginally significant for the cholesterol-HDL ratio (continuous), and significant for triglycerides (continuous). The loss of significance in these lipid variables in Models 4 and 6 is not unexpected because both of these models force statistical adjustment for serum lipid levels.

The adjusted analyses found significant positive associations for creatine kinase treated as a continuous variable. The adjusted results were marginally significant for creatine kinase in its discrete form. The serum amylase results found significant decreasing associations with lipid-adjusted dioxin and whole-weight dioxin. The result of the Model 6 analysis was marginally significant.

The adjusted results of the protein profile variables yielded several significant findings, including highly significant results ($p<0.005$ in at least one analysis) for α-1 antitrypsin, apolipoprotein B, C_3 complement, and transferrin. The Model 4 continuous analyses showed significant positive associations between lipid-adjusted serum dioxin levels and apolipoprotein B, C_3 complement, and transferrin, and also showed significant or marginally significant decreasing associations with α-1 acid glycoprotein, α-1 antitrypsin, and α-2 macroglobulin. The discrete analyses showed a marginally significant increasing association with abnormal high levels of apolipoprotein B, and significant or marginally significant decreasing associations with abnormal high α-1 antitrypsin, abnormal low C_3 complement, and abnormal low transferrin.

The adjusted Model 5 analyses for the protein profile variables showed essentially the same significant associations with whole-weight dioxin as were found in Model 4 with lipid-adjusted dioxin, but with stronger relationships (i.e., lower p-values). The only differences between Models 4 and 5 were that the association between whole-weight dioxin and α-1 acid glycoprotein was not significant and that the Model 5 associations with abnormal high α-1 antitrypsin and abnormal high apolipoprotein B were significant, rather than only marginally significant. In addition, there was a highly significant positive association between whole-weight dioxin and C_4 complement that was not significant for lipid-adjusted current dioxin.

The adjusted Model 6 analyses revealed fewer significant results than were revealed in Models 4 and 5 but the direction of the results was consistent among models. Significant results were revealed for α-1 acid glycoprotein (continuous), α-1 antitrypsin (continuous), α-2 macroglobulin (continuous), C_3 complement (continuous), and transferrin (continuous and discrete). The Model 6 analysis also revealed a significant inverse relationship with haptoglobin in its discrete form, which was not significant in either Model 4 or Model 5.

Overall

The analyses of the historical variables revealed significant or marginally significant inverse relationships with jaundice in all models except Model 2. Ranch Hands were at a marginally decreased risk of jaundice relative to the Comparison group, and the history of jaundice decreased significantly with current levels of dioxin. By contrast, the analysis of the category of other liver disorders revealed significant increasing associations with estimated initial dioxin exposure and current levels of serum dioxin, but the Ranch Hand versus Comparison group contrast was not significant. The other liver disorders category is

comprised mostly of elevated laboratory tests measured at previous AFHS examinations and does not represent a specific disease or condition.

In the analyses of the laboratory variables, the Model 1 group contrasts revealed several isolated statistically significant findings, but overall the gastrointestinal health of the Ranch Hand and Comparison groups did not differ substantially. Similarly, for the serum dioxin analyses, the adjusted Model 2 analyses detected few significant associations with estimated initial dioxin, and the adjusted Model 3 analyses revealed few consistent significant Ranch Hand dioxin category versus Comparison group contrasts.

The Model 4, 5, and 6 serum dioxin analyses detected many significant associations between the dependent laboratory variables and current dioxin, both lipid-adjusted and whole-weight. Significant associations were noted for some of the enzymes, the lipid and carbohydrate indices, and for several of the proteins. Alkaline phosphatase was not associated significantly with dioxin (Models 2, 4, 5, and 6), but the Model 1 and Model 3 analyses detected significant group differences between the Ranch Hands and Comparisons.

CONCLUSION

The gastrointestinal assessment found isolated statistically significant Ranch Hand versus Comparison group differences, but overall the health of the two groups did not differ substantially. The serum dioxin analyses indicated that estimated initial dioxin exposure was generally not associated with historical liver disorders or current laboratory measurements; however, the analyses revealed that current dioxin levels were often highly associated with lipid-related health indices such as cholesterol, HDL cholesterol, the cholesterol-HDL ratio, and triglycerides, as well as with some of the hepatic enzymes (ALT and GGT) and proteins. These seemingly discordant results may be explained in part because the initial dioxin analyses adjusted for differential half-life elimination related to percent body fat, while no adjustment was made in the analyses of current dioxin. However, these significant findings may be the result of a subclinical dioxin effect on lipid metabolism.

CHAPTER 13
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